United States
Department of
Agriculture

Forest Service

United States
Department of
the Interior

**Bureau of Land
Management**

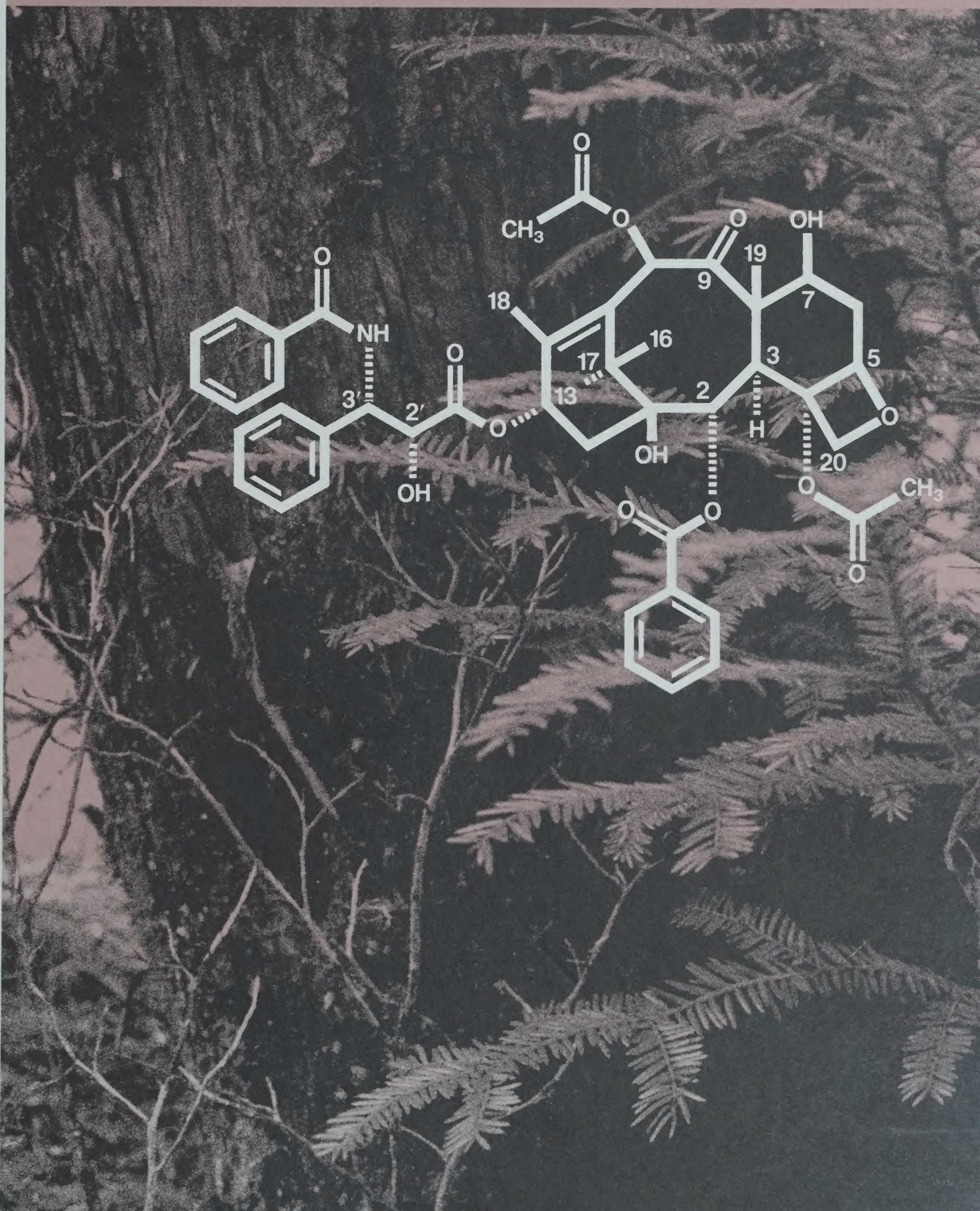
United States
Department of
Health and
Human Services

**Food and Drug
Administration**

Pacific Yew

Draft Environmental Impact Statement

JANUARY, 1993 ☐ **Appendices**



Appendices

Table of Contents

Appendix A

Public Involvement

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Public Involvement

Philosophy

Public involvement has been an integral part of the Pacific yew environmental impact statement (EIS) from the early stages to the present. According to NEPA (the National Environmental Policy Act), public issues must be addressed early in the process of preparing an EIS.

We used a number of public involvement methods. Our basic technique, which fit our philosophy, was "fish bowl planning." We attempted to make our decision-making process transparent to the public, to think out loud in front of everyone. We did this by first identifying all those who would or could be interested in the project, locally, nationally, and world-wide. We then sent letters and press releases, made telephone calls, attended meetings, produced and mailed newsletters, and analyzed the responses we received.

The public not only told us what the issues were, but also suggested items the alternatives should include, and what could be done to mitigate impacts on the environment.

The team gathered issues and suggestions and continued to process responses throughout the project. The public comments were used to help the team analyze the data, then formulate and evaluate alternatives, and recommend one.

Initial Issue Gathering

The Pacific yew newsletter was the main vehicle we used to gather public issues surrounding the harvest of Pacific yew from federal lands for the production of the cancer-fighting drug, taxol. The newsletter included a section for readers' comments to be returned to us.

Members of the Pacific Yew EIS team also met with various groups to discuss yew, taxol, and the EIS. On other occasions team members presented formal or informal talks on these subjects and used these opportunities to gather comments.

Response to December 1991 Pacific Yew Newsletter

The first Pacific Yew Newsletter, December 1991 (see the end of this appendix for a copy) was distributed in late December and early January to more than 20,000 citizens, groups, local governments, businesses, agencies, research facilities, hospitals, and universities. We asked for issues and concerns regarding the harvest of Pacific yew on national forest and Bureau of Land Management lands.

Most readers wanted us to harvest yew for the production of taxol, but at the same time protect the Pacific yew species and its environment; this was the major issue. Other comments concerned the "how to's," suggestions for ways we could approach solving the problem of how to provide taxol and protect the yew and its ecosystem. We grouped the comments into the following categories listed here, beginning with the category that received the largest number of comments:

Number of Comments	Comment Categories
Issues	
277	Provide material from the Pacific yew tree for the production of taxol for the treatment of cancer patients.
	Protect the yew species.
	Protect the ecosystem.
Suggestions	
211	Establish a sustainable level of collection—analyze minimum to maximum amounts.
172	Consider social, cultural, and tribal impacts of collecting yew.
166	Regenerate yew— plant and manage for natural regeneration.
139	Consider the economic impacts of yew collection on timber production, local employment, and sustained forest ecology to ensure future supplies of taxol and other possible drugs, and agreements for taxol production.

125	Establish areas of collection— decide whether or not to enter set-aside areas such as wilderness, spotted owl habitat, Research Natural Areas, and roadless areas; decide whether or not to build new roads for access; and concentrate collection in certain areas or spread collection over wide areas.
119	Establish collection methods— partially or wholly strip bark or fell trees; collect needles and twigs.
115	Utilize the yew completely— all bark, twigs, needles, and wood.
112	Develop other sources of taxol as soon as possible.
107	Stop theft and illegal harvest.
30	Miscellaneous.

Number	**Categories of Respondents**
621	Individuals and families
62	Interest groups
55	Businesses
29	Other agencies
24	Forest Service
21	College, universities, research
17	Medical professionals
5	Newspapers, radio, television reporters
834 Total	

Number	Geographic Distribution
475	Oregon
156	Washington
113	California
33	Idaho
11	Montana
6	Arizona
5	Utah
4	Maryland
4	Pennsylvania
4	Washington, DC
3	Canada
3	New York
3	Virginia
2	Colorado
2	Illinois
1	Hawaii
1	Iowa
1	Kansas
1	Massachusetts
1	Michigan
1	Minnesota
1	New Hampshire
1	New Jersey
1	Tennessee
1	Wisconsin
834 Total	

Issues and Suggestions

Provide material from the Pacific yew for taxol: Most people who responded want material from the Pacific yew to be available for the production of taxol and its use in clinical trials and treatment of ovarian and possibly other cancers. Some say saving human lives should be top priority; yew harvests should be maximized regardless of environmental impacts and wilderness and roadless areas should be opened for yew collection. Others say, although taxol should be made available, the yew tree and the ecosystem are important in themselves and for future generations and deserve protection; the harvest of yew for taxol should proceed with care, caution, and safeguards. **Issue**

Protect the ecosystem: People who commented want protection for the yew's ecosystem in order to ensure forest diversity. They want studies of the role yew plays in its community and the impact of yew harvest; some feel the forest has already been ruined by harvests. A major concern within ecosystem protection is the old growth or ancient forests; people want to protect and sustain ancient forests for future generations and for the unknown resources they may contain. Other concerns regarding the health of the ecosystem are for protection and understanding of: **Issue**

Wildlife, including deer, elk, moose (Idaho and Montana), birds, insects, the northern spotted owl and other threatened or endangered species; riparian zones, watersheds, and fish habitat; plants, including fungi; soils and soil organisms; and aesthetics.

Protect Pacific yew and maintain its genetic diversity: The concern is for careful management to protect the Pacific yew and its gene pool, balancing short- versus long-term needs for taxol. People want studies of yew in order to understand how to maintain the population and provide a viable gene pool for the future. With recent reports of infection of small amounts of yew trees with the root disease *Phytopthora lateralis*, found in Port-Orford-cedar, people want to know what steps can be taken to protect yew. **Issue**

Suggestion **Analyze and establish a suitable and sustainable level of harvest and taxol production:** This issue refers to the need for an accurate inventory of Pacific yew and its range in order to avoid over-harvesting, and to carefully manage for present needs and future generations.

Suggestion **Consider cultural, social, spiritual, and tribal values of yew:** Most people who responded were in favor of utilizing a balanced system of harvest while preserving the yew at historic levels, and giving consideration to multiple use and whole-ecosystem health. Many people felt that more attention should be given to the spiritual, cultural, and historical value of the yew. Some said that because Native Americans have a long tradition of using the yew for its healing powers, they should be guaranteed continued access to the tree. At least two respondents suggested getting direct tribal input for the EIS. Several people felt that the yew is sacred, and no harvesting of wild stands should take place. A significant number of others, however, said saving human lives should be top priority. Many felt yew harvests should be maximized regardless of environmental impacts. Some said they would like to see wilderness and roadless areas opened for yew collection.

Suggestion **Plant and manage for natural regeneration of Pacific yew:** In this case, people who commented were concerned about protecting the Pacific yew as a future resource. Most who commented agreed with harvesting yew trees for taxol, as long as sound reforestation practices that allow for natural regeneration or call for replanting are in place, and that nursery propagation efforts continue.

Suggestion **Consider the economic effects of yew collection on resources, economies, and future options:** Here, many people commented that maintaining a sustained forest ecology is essential for ensuring the future of taxol and other important drugs yet to be discovered.

A significant number of people said they think the agreement with Bristol-Myers Squibb company is "monopolistic," and that many companies, not just one, should benefit from taxol production.

The economic impacts of yew harvest and bark collection on the timber industry was another area of concern. Several people suggested that yew harvesting take place only in active timber sale areas. Some expressed concern over whether yew harvest and bark collection projects are used to provide jobs for local residents, especially in areas where there are a significant number of displaced timber workers.

Establish and define areas of collection or reserve areas: In this issue the number one public concern is the Forest Service treatment of set-aside areas. Sentiment is divided between those favoring absolutely no harvest in any set-aside area— Research Natural Areas (RNAs), wilderness, and Owl Conservation Areas (OCAs); limited harvest in these areas; and those favoring comprehensive harvest of yew wherever it is found in whatever quantity needed. Many people think that old growth forests should be left alone, although minimum intrusion may be allowed for research and inventory purposes.

Suggestion

Establish collection methods: In this case, many people want to know what kinds of yew harvest methods will be allowed, and how harvests will be incorporated into existing forest management prescriptions. Some said efficient collection methods should be established to ensure full utilization of the tree. Others said harvest methods that result in the death of the tree should be discontinued. Several people asked whether the yew trees can survive if they are partially stripped of their bark. A small number of respondents said only the needles and twigs should be collected. At least two people asked for a definition of "harvest" in regards to the yew.

Suggestion

Utilize all parts of harvested yew: Most people who commented want the whole yew tree to be used if the bark is going to be collected. They suggest it be used (perhaps commercially, for a fee) for fence posts, fire wood, bows, musical instruments, ornamental wood working, tool handles, and lumber.

Suggestion

Many people are concerned about waste of the tree during the harvesting process and want all bark from large and small limbs to be collected; they don't want to see the remaining tree burned or left to rot. Many want the small branches and needles to be used as well as the bark; some suggest collecting needles instead of bark in order to save the trees. Others would like to see the entire tree used for the extraction of taxol.

Suggestion **Develop other sources of taxol as soon as possible:** Many people called for the development of other sources of taxol as soon as possible, to avoid the burden on the yew species and the impacts of a long-term harvest program.

Many wanted to see a progress report on the development of other sources of taxol through synthesis, semisynthesis, cell culture, nursery propagation, heartwood extraction, and needle extraction.

Some people feel the Forest Service and BLM should fund research into alternate methods of producing taxol. Several say that taxol will soon be synthesized and the need for yew harvest will diminish. A few people asked what will become of the yew when it is no longer desired for its taxol.

Suggestion **Stop theft and illegal harvest of yew:** Many people expressed concern about the theft and illegal harvest of wild yew trees. Most wanted to know how illegal harvest would be stopped, and what kinds of punishment poachers would face if caught. Many felt there should be serious consequences for stealing yew trees. Some people questioned how to protect wild yew trees on their private lands. At least one respondent suggested using public awareness to monitor poaching and discourage theft.

Suggestion **Miscellaneous comments:** People expressed the following concerns and thoughts: After years of treating Pacific yew as a "weed" tree, we now find it to be a "lifesaver." We should research any other species of *Taxus* throughout the United States and the world. One never knows what could be found. We need to be extremely cautious about labeling plants as "trash." How many other species have potential lifesaving cures? We won't know

without thorough research starting back 10,000 years ago to the present era. Included in this research should be: identify high-yield and single yew tree populations; what age and/or time of year is Pacific yew richest in taxol-producing molecules; and the concept of "taxol farms" and how much could be produced this way. Pacific yew harvests could be taxed to help pay for this and other taxol research.

There is a question of whether or not an EIS is really necessary. If necessary, the EIS should be concise and in layman, not technical terms. Cost of the yew program is of concern and the public expects the Forest Service to be proactive and share whatever information there is, good or bad.

There is public misunderstanding of the word "harvest." There is some feeling that use of this word means the Forest Service will cut down every Pacific yew that can be found. A more value-less word would be preferred.

Will excessive environmental controls impact mining and mineral rights on public lands, and if so, how.

If the connection between taxol and cancer has been known for years, the government should pressure the FDA to set up approval of taxol synthesis for human use. An unedited short paper should be done on synthesis, expected side effects, and production timelines by an organic chemist and a pharmacologist. These people could give the most recent up-to-date information.

Yew bark harvesters should be trained to recognize Pacific yew so that other trees will not be damaged through ignorance.

Response to February 1992 Newsletter

Our second Pacific Yew Environmental Impact Statement newsletter, dated February 1992, was mailed in early March (see the end of this appendix for a copy).

About 100 people wrote to us in response to the February newsletter. In summary, this is what readers said:

Many readers liked the information in the February newsletter and thought we were on track with the issues, with some exceptions from those who felt we've done and are doing a poor job with forests in general.

About 20 readers responded to the issue of whether or not to enter set-asides such as wilderness areas and Owl Conservation Areas by saying "no," don't enter these areas. In the words of one reader from Etna, California, "Such entry, harvest and yew removal would seriously disrupt other major values for these natural ecosystems...". On the other hand, two readers feel we should enter any areas where yew trees grow in order to get taxol for research.

Other common comments were:

- Continue to encourage the development of other sources of taxol.
- Protect the overall forest health and ecosystems for the future.
- Regenerate yew (work on propagation techniques).
- Maintain a sustained yield of yew.
- Concentrate on needle and twig harvest rather than bark.
- Utilize as much of the yew tree as possible for taxol.

Number of Comments	Comment Categories
56	Protect the ecosystem (riparian areas, wildlife, other plants, soil, fire cycles, old growth forests) and the Pacific yew gene pool (establish reserve areas or numbers of reserve trees).
22	Consider social, cultural and tribal impacts of collecting yew.
21	Establish areas of collection— decide whether or not to enter set-aside areas such as wilderness, spotted owl habitat, Research Natural Areas, and roadless areas; decide whether or not to build new roads for access; and concentrate collection in certain areas or spread collection over wide areas.
20	Develop other sources of taxol as soon as possible.
17	Establish a sustainable level of collection— analyze minimum to maximum amounts.
17	Utilize the yew completely— all bark, twigs, needles, and wood.
17	Consider the economic impacts of yew collection on timber production, local employment, sustained forest ecology to ensure the future supplies of taxol and other possible drugs, and agreements for taxol production.
12	Establish collection methods— partially or wholly strip bark or fell trees; collect needles and twigs.
12	Regenerate yew— plant and manage for natural regeneration.
11	Stop theft and illegal harvest.
23	Miscellaneous.

Number	Categories of Respondents
67	Individuals and families
9	Businesses
8	Interest groups
7	Other agencies
5	Medical professionals
4	College, universities, research
3	Forest Service
0	Newspapers, radio, television reporters
97 Total	

Number	Geographic Distribution
47	Oregon
17	California
16	Washington
5	Idaho
4	Montana
2	Arizona
1	Maryland
1	Michigan
1	New Hampshire
1	Utah
1	Washington, DC
1	Canada
97 Total	

Response to June 1992 Newsletter

Our third Pacific Yew Environmental Impact Statement newsletter, dated June 1992, was mailed in early July (see the end of this appendix for a copy).

A summary of the responses to the proposed alternatives described in this newsletter will appear in this appendix when the final EIS is published.

Appendix A

Newsletters

First Newsletter

December 1991

December 1991

Pacific Yew

ENVIRONMENTAL IMPACT STATEMENT

What's so important about the Pacific yew?

An often overlooked species in our western forests, the Pacific yew has recently emerged from obscurity. It is now a species in demand because of the discovery that it yields taxol, an anticancer drug found to be 30 to 35% successful in the treating of ovarian cancer patients that have not responded to previous treatment. Taxol has shown promise in the treatment of other cancers.

People are talking . . .

"Taxol's status as a hot new cancer drug has given researchers an opportunity to help solve a societal problem of pressing importance."
—Stu Borman, writer for Chemical and Engineering News

"For the short term we will be living with inadequate supplies of this drug, but in the long term the problem is going to be solved."
—Samuel Broder, National Cancer Institute director

"In the meantime, traditional plant sources must be used to meet immediate research needs."
—James C. Overbay, deputy chief of the Forest Service

"There will be rapidly increasing demand for taxol as we begin studies on use of the substance to treat other forms of cancer."
—Dr. Saul A. Schepartz of National Cancer Institute's Developmental Therapeutics Program

"It ought to be a firm message that there's been too much wastage and not enough management."
—Congressman Ron Wyden, commenting on "The Pacific Yew Act of 1991"

"If we expect to increase the production of taxol and conserve the yew species, we must proactively manage forests on the public lands."
—D. Dean Bibles, Oregon /Washington State Director of the BLM

"Optimize use for human beings, minimize environmental impacts."
—Diane Di Furia, Bristol-Myers Squibb Company

"The conflict is, there are no such lands where taxol production is the priority. The priority still remains the production of Douglas-fir wood fiber."
—Wendell Woods, Oregon Natural Resources Council

"I've had the conventional chemotheraphy for ovarian cancer, and it didn't work . . . Taxol may be my last hope."
—Sally Thane Christensen, "Is a Tree Worth a Life"

What Are the Effects of Collecting Yew? Or, Why this Environmental Impact Statement?

Since most of the Pacific yew available to supply bark (from which taxol is extracted) is found on federal lands managed by the USDA Forest Service and the US Bureau of Land Management, these agencies will prepare an environmental impact statement to analyze the effects of yew collection on the environment. The Forest Service is the lead agency; BLM, the National Cancer Institute, and the U.S. Food and Drug Administration are cooperating agencies.

In this EIS we will analyze the effects of harvest on the yew's ability to regenerate, its genetic diversity, and its place in forest ecosystems. We will propose, study, and weigh various harvest alternatives.

USDA Forest Service US Bureau of Land Management
U.S. Food and Drug Administration

We will focus on the short and long-term effects of a five-year harvest program. The need for yew bark from forest trees is expected to decrease as researchers find ways to extract taxol from needles and heartwood, propagate yew and extract taxol from clippings at yew nurseries, semi-synthesize and totally synthesize taxol and its related compounds, and produce taxol through tissue culture.

Possible Alternatives

Alternative yew harvest programs that we will propose in this EIS could cover various yew harvest levels — from no harvest at all to a high level. Methods of harvest and utilization of the tree could be important parts of each alternative. Concurrently, the Forest Service and the Bureau of Land Management are conducting yew surveys and inventories; these will help us estimate how much yew is present and help us analyze the impacts of alternate programs on the species. A technical team is preparing conservation guidelines for the Pacific yew.

The Future of Taxol Production

"Nobody owns the compound. We didn't patent it when we isolated it."
—Monroe E. Wall, chemist with Research Triangle Institute

Researchers at companies, universities, and agencies world-wide are working to develop taxol or a closely related drug from bark, needles, heartwood, yew nurseries, tissue culture, semi-synthesis and total synthesis.

Here is a partial list of some of the current research and development of taxol:

Rhone-Poulenc Rorer, a French pharmaeutical firm, has developed Taxotere, a taxol analog made by partial synthesis from a taxol precursor extracted from the needles of European yew, *Taxus baccata*.

The Weyerhaueser Company is propagating yew at a nursery in Washington. Forest Service nurseries near Carson, Washington, Medford, Oregon, and Coeur d'Alene, Idaho, and the Chico Tree Improvement Center in California are also working with yew propagation.

Researchers at the USDA Forest Products Laboratory in Madison, Wisconsin have successfully extracted taxol from Pacific yew heartwood.

Dr. Holton and co-workers at Florida State University are working on partial and total synthesis of taxol. Thirty or more other research groups across the US are also investigating synthesis of taxol.

BLM's Horning Seed Orchard near Molalla, Oregon is planning studies of the Pacific yew, including seed germination, rooted cuttings, and transplanting.

Edward Croom, Jr. of the Research Institute of Pharmaceutical Sciences at the University of Mississipppi is studying the possiblilities of taxol production from ornamental yews (*Taxus* spp) in nurseries.

The NaPro Company in Boulder, Colorado is extracting taxol from yew needles in research quantities, not yet approved for human use.

Phyton Catalytic Inc. of Ithaca, New York, and ESCAgenetics of San Carlos, California, are producing taxol and taxol-like compounds from yew cells grown in culture (tissue culture).

Apologies — Have we sent you more than one copy?

This is the first of a series of newsletters about the Pacific Yew Environmental Impact Statement (EIS). In an attempt to reach many people who may be interested in the project, we have used several mailing lists and you might receive more than one copy. If you do, we apologize; perhaps you could pass the extra copy to a colleague, friend, or neighbor.

Raising Your Taxus

In the EIS we will be analyzing the impact of harvesting Pacific yew (*Taxus brevifolia*) on National Forest and Bureau of Land Management forests in Washington, Oregon, Idaho, Montana, and northern California. These are the main National Forests and Bureau of Land Management Districts where yew trees are found.

National Forest

California
Klamath
Lassen
Mendocino
Plumas
Shasta-Trinity
Six Rivers
Tahoe

Idaho
Clearwater
Idaho Panhandle
Nez Perce

Montana
Flathead
Kootenai

Oregon
Mt. Hood
Rogue River
Siuslaw
Siskiyou
Umatilla
Umpqua
Willamette

Washington
Gifford Pinchot
Mt. Baker-Snoqualmie
Olympic

BLM Districts

Oregon
Coos Bay
Eugene
Medford
Roseburg
Salem

Idaho
Couer d' Alene

Please Call Us

If you have issues and concerns you would like to discuss with the team preparing this EIS, please contact Sally or Susan. The team is available to meet with individuals or groups.

Sally Campbell, Forest Service
Pacific Yew EIS team leader (503) 326-7755
Pacific Yew EIS Team
USDA Forest Service
P.O. Box 3623
Portland, OR 97208-3623

Susan Whitney, Forest Service
Pacific Yew EIS public involvement specialist
(503) 326-7733
Pacific Yew EIS Team
USDA Forest Service
P.O. Box 3623
Portland, OR 97208-3623

The following people can also answer your questions about Pacific yew:

Fred Page, Forest Service Pacific Northwest Region, yew coordinator, (503) 326-3538

Merril Davis, Forest Service Northern Region, yew coordinator, (406) 329-3334

Mike Srago, Forest Service Pacific Southwest Region, yew coordinator (415) 705-2697

Doug Daoust, Forest Service, interim yew conservation guidelines team leader, (503) 666-0700

Kent Tresidder, Bureau of Land Management, Oregon/Washington yew program coordinator, (503) 280-7070

Leslie Robinette, Bureau of Land Management, public affairs specialist, (503) 280-7031

Phillip G. Vincent, U.S. Food and Drug Administration, environmental assessment officer, (301) 443-4330.

Getting to Know Yew . . .

❑ A slow-growing evergreen tree or shrub

❑ Found in forests of the western U.S. and Canada

❑ Not a rare plant, but distribution is usually scattered except in a few locations; common in many riparian areas

❑ Wood is hard and prized for such items as fence posts, bows, lutes, and snowshoe frames

❑ Regenerates by sprouting from stumps; layering (putting roots down when branches meet the soil); and by seeds, probably transported by birds and browsing animals like deer, elk and moose

❑ Seeds are surrounded by a scarlet, juicy, berry-like cup called an aril

❑ Usually dioecious; the male flowers are on one tree, the female on another

❑ Some yews have been found to be monoecious, with male and female flowers on the same tree

. . . and Taxol

❑ Currently obtained by extraction from the bark of Pacific yew (*Taxus brevifolia*)

❑ The procedure for extraction is difficult, low yielding and expensive at present

❑ Three trees (10" in diameter) yield enough drug for one cancer patient (National Cancer Institute estimate)

❑ 500 patients are currently receiving the drug in clinical trials and compassionate use

❑ Discovered in 1963 as part of the National Cancer Institute-sponsored program to screen plants for medicinal properties

❑ 750,000 pounds of bark will yield about 25 kilograms of taxol, enough for some 12,000 patients

What's Next?

In the next issue of Pacific Yew we will summarize your comments, discuss the issues raised, explore more alternatives, and provide an update on yew inventories.

You Can Comment:

We are at the beginning stages of the EIS project. We need to know what issues you have regarding the harvest of yew on National Forest and Bureau of Land Management land. What concerns you? What should we address in the EIS? The issues you provide will be used to form and evaluate alternative harvest programs developed in the EIS.

Do you want to remain on the mailing list?

If you want to continue to receive information about the Pacific Yew EIS, please check the box and return this section.

Yes, I'd like to remain on the mailing list ☐

Please print

Name: ____________________

Address: ____________________

City, State, Zip: ____________________

USDA Forest Service
Pacific Yew EIS Project
P.O. Box 3623
Portland,OR 97208-3623

Fold on This Line

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Pacific Yew EIS Project
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Portland,OR 97208-3623

A Public Involvement

Second Newsletter

February 1992

February 1992

Pacific Yew

ENVIRONMENTAL IMPACT STATEMENT

Thank You for Commenting

We mailed about 23,000 Pacific Yew newsletters in late December asking for your comments regarding the collection of yew bark on National Forest and U.S. Bureau of Land Management land. We asked for concerns and issues to be addressed in the Pacific Yew Environmental Impact Statement. By mid-February we had received more than 700 comments.

In summary, your primary concern, with few exceptions is:

Collect Pacific yew *(Taxus brevifolia)* bark for taxol, but at the same time, protect the species and its ecosystem.

Considering this primary concern, these appear so far, to be the main items you want us to consider:

- ☐ Establish a sustainable level of collection — analyze a range of minimum to maximum levels.
- ☐ Establish areas of collection — decide whether to enter set-aside areas such as Wilderness, spotted owl habitat, Research Natural Areas, and roadless areas or to stay out of set-asides; decide whether or not to build new roads for access; concentrate collection in certain areas or spread collection over wide areas.
- ☐ Utilize the yew completely — all bark, twigs, needles, and wood.
- ☐ Establish collection methods — partially or wholly strip bark or fell trees; collect needles and twigs.
- ☐ Regenerate yew — plant and manage for natural regeneration.
- ☐ Stop theft and illegal harvest.
- ☐ Protect the Pacific yew gene pool — establish reserve areas or numbers of reserve trees.
- ☐ Protect the ecosystem — riparian areas, wildlife, other plants, soil, fire cycles, old growth forests.
- ☐ Develop other sources of taxol as soon as possible.
- ☐ Consider the economic impacts of yew collection on timber production, local employment, sustained forest ecology to ensure the future supplies of taxol and other possible drugs, and monopolistic agreements for taxol production.

Questions You Asked and Some Answers

Q. Can I grow yew? Should I grow yew? How? Where? Where can I buy yew seeds or seedlings?

A. Under most circumstances Pacific yew grows very slowly, so if you are thinking of growing it for future bark harvest, you'll have a long wait (70 to 100 years for a tree 8 to 10 inches in diameter). Growing yew for needle collection is uncertain at this time because of extraction difficulties and the fact that only taxol extracted from bark is approved for research and clinical trials by the Food and Drug Administration, although this could change. You might want to contribute to the genetic biodiversity of Pacific yew by preserving a small stand on your land.

Pacific yew regenerates by sprouting from a stump when the tree is cut, by layering (when one of its branches lies on the ground long enough to put down roots), and by seeds. Although nurseries such as Weyerhaeuser and several Forest Service and Bureau of Land Management nurseries are researching yew propagation, none of them are selling yew seeds or seedlings to the public. The Forest Service nurseries are only allowed to sell surplus stock to the public and probably won't be producing surplus Pacific yew for years to come. This regulation exists so that the federal government will not be in competition with private nurseries.

Although many private nurseries grow ornamental yew varieties for hedges and landscaping, few propagate Pacific yew. Without endorsing these to the exclusion of other growers we are not yet aware of, here are the addresses of two nurseries that propagate Pacific yew:

Special Trees P.O. Box 2238 Corvallis, OR 97339 (503) 758-7131	Green Hills Nursery 40805 Upper Nestucca Road Beaver, OR 97108 (503) 398-5965

Q. Can I collect bark? How? Where do I sell it?

A. A principal bark buyer is Hauser Northwest Inc., 78120 Highway 99S, Cottage Grove, OR 97424, (503) 942-9655. Hauser Northwest carries the contract to supply bark to Bristol Myers Squibb Company which has an agreement to supply taxol to the National Cancer Institute.

Q. What are the Forest Service and BLM doing to stop yew theft?

A. The Forest Service is offering a $10,000 reward for information leading to the arrest and conviction of anyone who harvests Pacific yew bark illegally on National Forest lands.

Thieves of yew bark on BLM-managed lands may face multiple felony theft charges, including a prison term, a fine of $10,000, and seizure of bark, tools, and vehicles. You can report yew theft to BLM law enforcement agents by calling 1-800-333-7283.

Both agencies have either a permit or sale contract system for the legal harvest of bark on federal lands.

Q. Is there a Pacific yew inventory? If so, what is its status?

A. Yes, there are several Pacific yew inventories underway.

During the 1992 field season (March to October), Forest Service crews in the Pacific Northwest Region (Oregon and Washington) will complete an inventory of Pacific yew (begun in 1991) on seven national forests — Gifford Pinchot, Mt. Baker/Snoqualmie, Mt. Hood, Rogue River, Siskiyou, Umpqua, and Willamette. In the Northern Region (which includes the yew forests in Idaho and Montana), the Forest Service is inventorying 100,000 acres of the Nez Perce National Forest which contain over 80% of the tree size yew in the region.

Additional information will be provided by a survey of Forest Service lands in northern California (the Klamath, Six Rivers, Plumas and Tahoe National Forests), and by analysis of existing data for state and private lands in Oregon, Washington, Idaho, Montana, and northern California.

The BLM will conduct a Pacific yew inventory on its western Oregon forest lands, where some 90% of the species under BLM management is estimated to occur. Maps delineating three levels of yew occurrence will be completed by field staff in April. Field sampling will begin shortly after that and inventory results are anticipated by the end of December.

Private Nurseries are Researching Yew Propagation for Taxol Production

The development of alternative sources of taxol is being pursued actively by both the National Cancer Institute and Bristol-Myers Squibb. The CRADA (Cooperative Research and Development Agreement) requires them to develop alternative sources as soon as possible.

The Weyerhaeuser Company, in an agreement with the Bristol-Myers Squibb Company, is engaged in research and cultivation of domestic yew to provide a reliable, long-term, affordable supply of taxol. At the Weyerhaeuser Regeneration Facility near Rochester, Washington, local workers have been hired to sort, wash, trim, and "stick" cuttings from various yew species into growing containers that look somewhat like ice cube trays. The idea is to grow yew seedlings in the greenhouse and in nursery beds for three or four years and then use the biomass — stem, twigs, needles, and perhaps roots — for the extraction of taxol. Weyerhaeuser hopes to grow 5 million rooted yew cuttings in 1992.

Presently, the bark of the Pacific yew is the only FDA approved source of taxol for research and clinical use. If the Weyerhaeuser yew cultivation project is successful, it may present a solution to the issues surrounding the collection of Pacific yew bark in the wild.

In a similar vein, the National Cancer Institute transferred funds ($250,000) to the USDA Cooperative State Research Service which then added $60,000 of its own to provide $310,000 to Zelenka Nursery in Michigan; Zelenka Nursery is coordinating the project with the University of Mississippi, Ohio State University and several other nurseries. Together, these groups are researching the best methods for harvesting and drying needles and twigs from ornamental yew (*Taxus media v. hicksii*). They will supply dried biomass to the National Cancer Institute. NCI will contract the extraction of taxol from the biomass and then transfer the material to Bristol-Myers Squibb for final purification of taxol; Bristol-Myers Squibb will then forward to the NCI clinical supplies of taxol.

Please Call Us

If you have issues and concerns you would like to discuss with the team preparing this EIS, please contact Sally or Susan. The team is available to meet with individuals or groups.

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Kent Tresidder, Bureau of Land Management, Oregon/Washington yew program coordinator, (503) 280-7070

Leslie Robinette, Bureau of Land Management, public affairs specialist, (503) 280-7031

Phillip G. Vincent, U.S. Food and Drug Administration, environmental assessment officer, (301) 443-4330.

Getting To Know Yew... 1/
(continued from December 1990)

- ❑ Yew is a slow growing conifer rarely exceeding 24 inches in diameter and 60 feet in height; its needles are dark green, two ranked, and spirally arranged on the twigs; the bark is purplish, papery thin, and scale-like; the crown tends to be ragged and lopsided.

- ❑ Yew is often found in the understory of old-growth Douglas-fir forests, but it also occurs in some stands less than 10 years old; it is considered a late seral to climax species (a late to final species in a community of plants achieved through successful adjustment to an environment).

- ❑ It is present in an extremely large number of plant communities.

- ❑ In western Oregon and Washington, yew often grows with western hemlock, Pacific rhododendron, and beargrass.

- ❑ It is found over a wide range of moisture and temperature conditions and elevations, even growing in non-forest areas such as avalanche chutes, talus and scree slopes, and rocky cliffs.

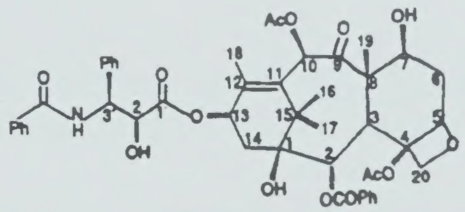
- ❑ The establishment of Pacific yew is influenced by fire history, browsing animals, its ability to compete successfully, climatic conditions, and seed crops.

- ❑ It is extremely variable in growth form (shrubs to trees) and in taxol content

1/ Facts from USDA Forest Service, Draft "An Interim Guide to the Conservation and Management of Pacific Yew."

...and Taxol

- ❑ Taxol belongs to a group of compounds called taxanes; it is one of the most complex taxanes known.



- ❑ Due to its molecular complexity, total synthesis of taxol has yet to be achieved.

- ❑ Taxol can be partially synthesized from a precursor, 10-deacetyl baccatin-III, found in needles of *Taxus baccata*, English yew, and from baccatin III, found in virtually all yew species.

- ❑ Taxol inhibits cell division, and therefore the growth of cancer cells, by preventing microtubule disassembly necessary for completion of cell division. (A microtubule is any of the minute cylindrical structures in cells that are widely distributed in protoplasm and are made up of protein subunits).

What's Next?

- ❑ A summary of "An Interim Guide to the Conservation and Management of Pacific Yew."
- ❑ An update on the inventory.
- ❑ A summary of proposed alternatives for yew collection.

You Can Comment:

We invite you to comment as we prepare the environmental impact statement. How are we doing? Have we summarized the issues fairly? What else should we consider as we develop proposals for yew bark collection?

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A Public Involvement

Third Newsletter

June 1992

June 1992

Pacific Yew

ENVIRONMENTAL IMPACT STATEMENT

"What makes taxol so precious is its promising ability to shrink cancer tumors."
— Michael Unger, Medford Mail Tribune

Thanks Again For Commenting

We appreciate your interest in the Pacific Yew Environmental Impact Statement (EIS) project and thank you for writing to us. This newsletter is the third in a series we will publish during the duration of the EIS project.

More than 800 readers sent us comments in response to the December newsletter regarding the issues we should consider while analyzing yew collection programs for taxol production. We published these issues in the February newsletter.

About 100 people wrote to us in response to the February newsletter. In summary, this is what readers said:

Many readers liked the information in the February newsletter and think we're on track with the issues, with some exceptions from those who feel we've done and are doing a poor job with forests in general.

About 15 readers responded to the issue of whether or not to enter set-asides such as Wilderness Areas and owl Habitat Conservation Areas by saying "no, don't enter these areas." In the words of one reader from Etna, California, *"Such entry, harvest and yew removal would seriously disrupt other major values for these natural ecosystems..."* On the other hand, two readers feel we should enter any areas where yew trees grow in order to get taxol for research.

Other common comments (5 or more readers agreed) were:

- ❑ Continue to encourage the development of other sources of taxol
- ❑ Protect overall forest health and ecosystems for the future
- ❑ Regenerate yew (work on propagation techniques)
- ❑ Maintain a sustained yield of yew
- ❑ Concentrate on needle and twig harvest rather than bark
- ❑ Utilize as much of the yew tree as possible for taxol

We're Counting Yew — Update on the Inventory

"Get an accurate inventory."
— Comment from a reader in Gilchrist, Oregon.

At this point in time, we have several sources of information we can use to estimate the amount of Pacific yew in Washington, Oregon, Idaho, Montana, and northern California.

For the draft EIS we will use:
The Pacific Northwest Region Yew Inventory: This began in the late summer of 1991 in six national forests in Washington and Oregon. These forests were: Mt. Baker-Snoqualmie, Gifford Pinchot, Mt. Hood, Willamette, Umpqua, and Rogue River.

The Northern Region Forest Inventory: This tallied Pacific yew in the Northern Region, including northern Idaho and Montana.

Bureau of Land Management (BLM) Inventory: This tallied yew on BLM lands.

The Forest Inventory Analysis: A Forest Service research station inventory that tallied Pacific yew on state and private lands in Oregon, Washington, Idaho, Montana, and California.

Based on Pacific yew inventory information gleaned from these sources, we will estimate the amount of yew available for harvest in each alternative. Knowing the estimated numbers of yew will help us analyze the effects of implementing each alternative. We will show the results in the draft EIS to be published in October 1992.

For the final EIS we will use:
The Pacific Northwest Region Inventory: Crews continue to inventory Pacific yew in seven national forests (now including the Siskiyou).

The Nez Perce Yew Inventory: In the Northern Region yew is being inventoried on the Nez Perce National Forest because it contains a majority of yew in this region.

The Pacific Southwest Region Inventory: A yew inventory of four national forests in northern California will begin this summer.

The BLM Yew Inventory: A yew inventory in districts of western Oregon.

By August all inventory sampling should be completed; then work begins to summarize the data. We will use that data to update the analysis and comparison of alternatives for the final EIS to be published in March 1993.

Questions You Asked and Some Answers

Q: Will yew be harvested in Wilderness Areas and Natural Research Areas?

A: No. None of the alternatives propose yew harvest in these set-aside areas.

Q: Will yew be harvested in spotted owl HCAs (Habitat Conservation Areas)?

A: We don't know at this time. We will analyze the impacts of harvesting yew in HCAs in two alternatives, E and G, using information from owl biologists. The Regional Forester and BLM State Director will make the final decisions when they choose the alternative to be implemented for their agencies.

Q: How many patients will be treated with taxol in 1992?

A: According to the National Cancer Institute, possibly 8,000 to 10,000 patients may receive taxol treatment in 1992.

Q: What's happening with research into taxol production from other sources?

A: More than thirty different groups are continuing to work on the production of taxol, ranging from the use of biomass collected from nurseries and wild species growing world-wide, to synthesis, semi-synthesis, and cell culture. So far, none are producing commercial amounts, although substantial progress has been made.

So Far, These Are The Alternatives We're Proposing

What follows is a brief description of each alternative.

Alternative A (the No Action alternative)

Harvest areas:
(1) None

Harvest percentages:
(1) 0%

Alternative B

Harvest areas:
(1) Clearcut and shelterwood sale units only

Harvest percentages:
(1) 100% harvest

Alternative C

Harvest areas:
(1) Clearcut and shelterwood sale units
(2) Partial-cut sale units and non-sale areas

Harvest percentages:
(1) 100% harvest in clearcut and shelterwood sale units
(2) 25% harvest in partial-cut units and non-sale areas

Alternative D

Harvest areas:
(1) Clearcut and shelterwood sale units
(2) Partial-cut sale units and non-sale areas

Harvest percentages:
(1) 100% harvest in clearcut and shelterwood sale units
(2) 50% harvest in partial-cut sale units and non-sale areas

Alternative E

Harvest areas:
(1) Clearcut and shelterwood sale units
(2) Partial-cut sale units and non-sale areas
(3) Habitat Conservation Areas (HCAs)

Harvest percentages:
(1) 100% harvest in clearcut and shelterwood sale units
(2) 50% harvest in partial-cut units and non-sale areas
(3) Some harvest in HCAs, to be determined by consultation with owl biologists

Alternative F

Harvest areas:
(1) Clearcut and shelterwood sale units
(2) Partial-cut sale units and non-sale areas

Harvest percentages:
(1) 100% harvest in clearcut and shelterwood sale units
(2) 75% harvest in partial-cut sale units and non-sale areas

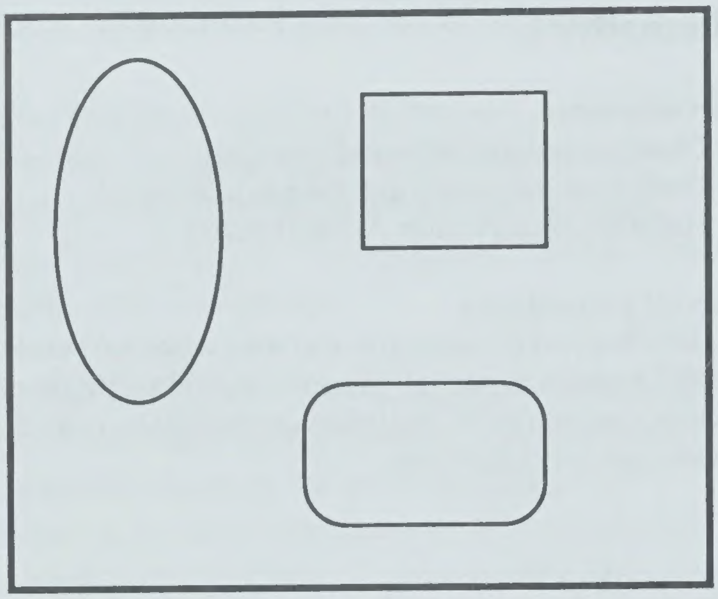
Alternative G

Harvest areas:
(1) Clearcut and shelterwood sale units
(2) Partial-cut sale units and non-sale areas
(3) HCAs

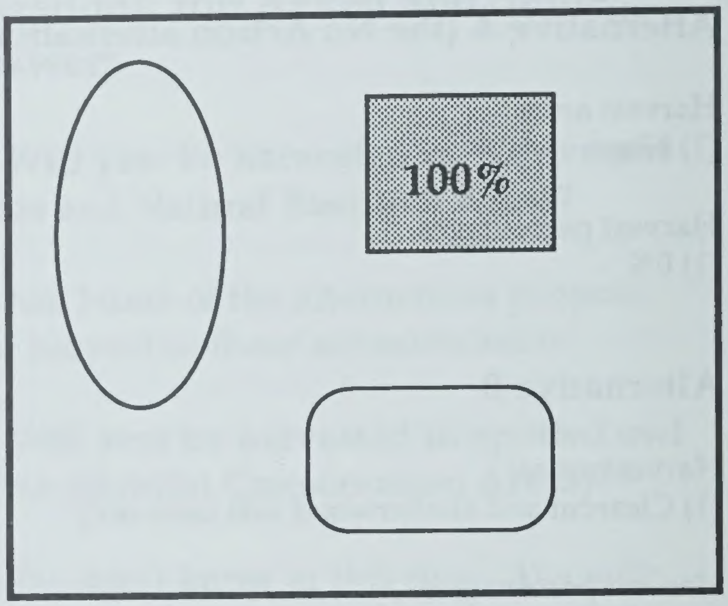
Harvest percentages:
(1) 100% harvest in clearcut and shelterwood sale units
(2) 75% harvest in partial-cut sale units and non-sale areas
(3) Some harvest in HCAs, to be determined by consultation with owl biologists

This is a simplified illustration of the alternatives showing the types of areas where Pacific yew could be harvested and the percent that could be harvested from that area.

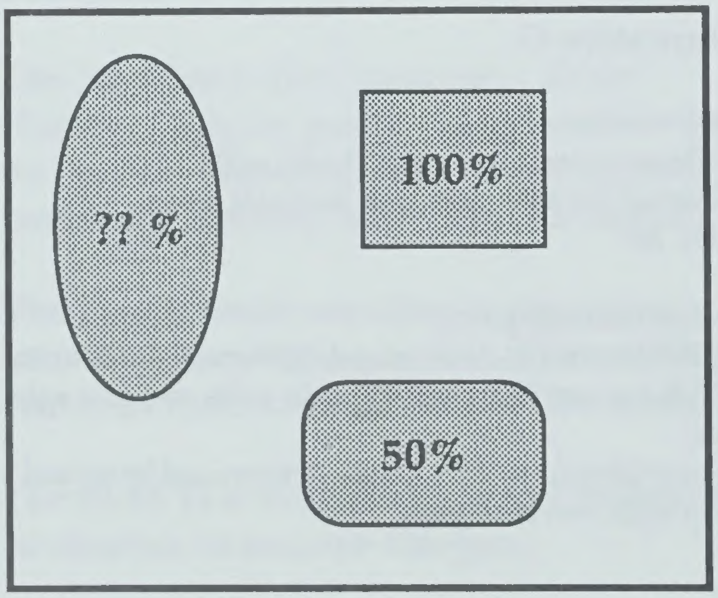
Alternative A:



Alternative B:



Alternative E:



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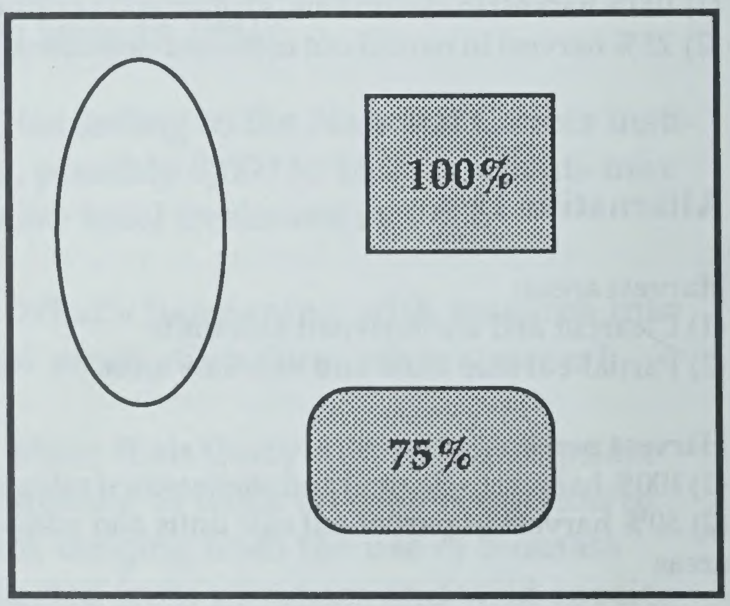
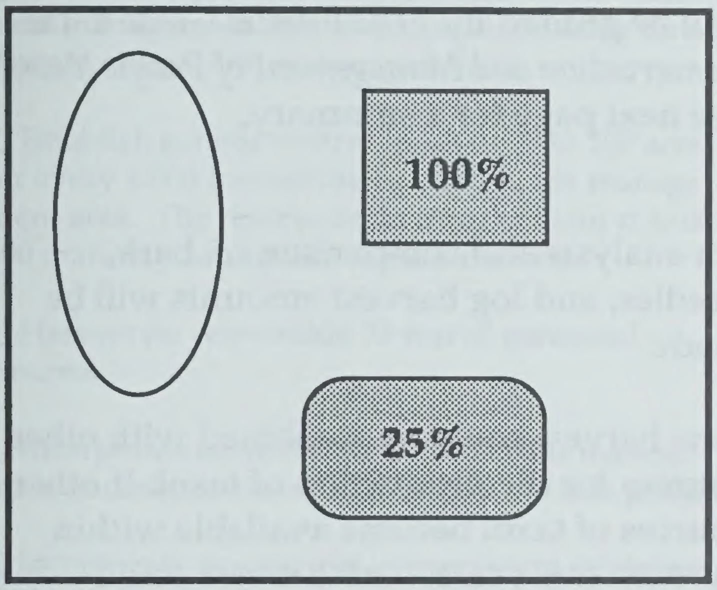
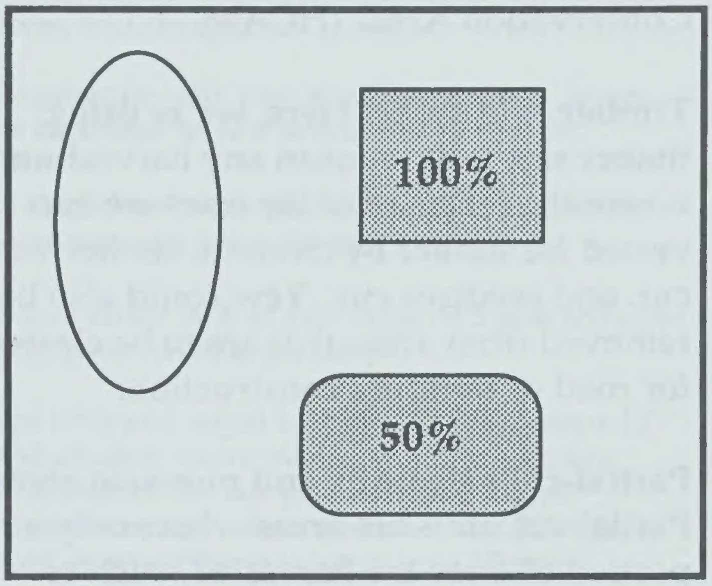


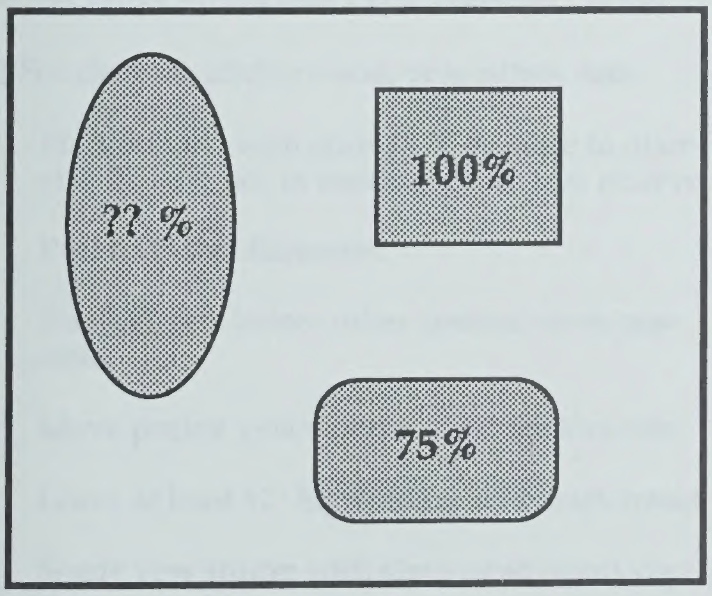
Alternative C:



Alternative D:



Alternative G:



Shading = Pacific yew will be harvested.

Percent = amount of yew that will be harvested

= HCA (Habitat Conservation Area) for spotted owls.

= Timber sale units - clearcut, shelterwood, or seedtree harvest.

= Partial- cut units such as thinning or uneven-aged cuts and non-sale areas where yew harvest is allowed in the Forest Plans.

Differences

Harvest areas: The alternatives differ from each other in terms of areas yew could be harvested from: timber sale units; partial-cut sale units and non-sale areas; or Habitat Conservation Areas (HCA's).

Timber sale units: Here, we're using timber sale unit to mean any harvest unit where the majority of the trees are harvested for timber by clearcut, shelterwood cut, and seedtree cut. Yew could also be removed from areas that are to be cleared for road or building construction.

Partial-cut sale units and non-sale areas: Partial-cut units are areas where only a portion of trees are harvested, such as salvage sales or uneven-aged harvest sales. Non-sale areas are areas where no timber sales have occurred or are planned and where the Forest Plans or BLM guidelines allow for yew harvest.

Habitat Conservation Areas (HCAs): These are areas set aside for the northern spotted owl — contiguous blocks of habitat to be managed and conserved for breeding pairs, connecting corridors, and distribution of spotted owls.

Percentages of harvest: Alternatives also differ in the percentage of yew harvest allowed in the partial-cut and non-sale areas. We will look at removal of 0%, 25%, 50% and 75% of the yew trees greater than 3 inches in diameter at the stump.

Similarities

In all alternatives (except A) you will find the following:

Yew harvest, protection, and regeneration will be guided by *"The Interim Guide to the Conservation and Management of Pacific Yew."* See next page for a summary.

An analysis and comparison of bark, needles, and log harvest amounts will be made.

Yew harvest could be combined with other sources for the production of taxol: If other sources of taxol become available within the next five years, bark harvest could decrease.

Summary—
"The Interim Guide to the Conservation and Management of Pacific Yew"

These guidelines will govern the 1992 harvest of Pacific yew on National Forest lands.*

❑ Harvest no yew if sites of 20 to 100 acres within a local management area of about 20,000 acres do not contain at least 500 mature yew trees.

❑ Establish genetic reserve areas of 20 to 100 acres for every 2,000 foot elevation band in the management area. The reserve areas must contain at least 500 mature yew capable of reproduction.

❑ Harvest no yew within 75 feet of perennial streams.

❑ Incorporate current Port Orford cedar management guidelines where Port Orford cedar is present.

❑ Incorporate current owl management guidelines within 1/4 mile of northern spotted owl nest, outside of Habitat Conservation Areas. No harvest in HCA's except where sales exist.

❑ Consult local game biologist if in deer, elk and moose winter range.

❑ Follow standards and guidelines for management area "21" of the Nez Perce Forest Plan and related information in this "Interim Guide" if in moose winter range on the Nez Perce National Forest.

❑ For clearcut, shelterwood, or seedtree cuts:

Harvest yew with stumps 3" or more in diameter that are not in residual green tree reserve.

Peel to 1" top diameter.

Harvest yew before other species when possible.

Move peeled yew wood to a secure location.

Leave at least 12" high stump with bark intact.

Shade yew stump with slash or adjacent vegetation.

Protect and retain 50% of residual yew stumps, trees, and shrubs.

Regenerate with yew sprouts, cuttings, layers, or seedlings to yew levels before harvest.

❑ For partial-cut sales (thinning, salvage, unevenage) and non-sale areas for tree form yew.

Leave either 50% of yew trees or 5 yew trees per acre (whichever is greater).

For bark and wood harvest: Leave stumps 12" and shaded; move peeled wood to a secure location; do not cut yew with less than 3" diameter stump; do not reenter stand for yew bark or wood harvest for at least 10 years.

For foliage harvest: Distribute foliage removal evenly through crown; do not harvest foliage from trees less than 1" diameter breast high; reenter stand only after foliage re-growth has occurred and re-harvest foliage from same trees each time;

❑ For partial-cut for shrub form yew:

Leave 50% of yew shrub cover evenly distributed.

For bark and wood harvest: Leave 12" high or long, shaded stumps with bark intact; do not cut shrubs with a stump less than 1" diameter at 12" from the ground; do not reenter stand for bark harvest for at least 10 years.

For foliage harvest: Remove no more than half the foliage, evenly distributed throughout the crown; do not harvest foliage from shrubs with stumps less than 1" in diameter 12" from the ground; do not reenter stand for foliage harvest for at least 5 years.

* The 1992 yew harvest on BLM lands will be guided by *"FY'92 Pacific Yew Administrative Policies."* See next page for a summary.

The 1992 Pacific Yew Collection Season Is Here

"The production of taxol as a cancer fighting agent continues to be an item of National interest and concern. The Forest Service must make sure that there is an opportunity to utilize as much Pacific yew as possible for the production of taxol." -- F. Dale Robertson, Chief of the Forest Service

"I consider the Pacific yew a top priority for the BLM. Wasting this resource, for any reason, will not be tolerated." -- Cy Jamison, BLM Director

As last season's Pacific yew bark collection progressed, we learned about the process through successes and failures. We continue to find ways to improve. The Chief of the Forest Service, the Pacific Northwest Regional Forester, the Director of Timber Management, and the BLM Oregon State Director have sent letters to the national forest supervisors and BLM district managers with new direction for the Pacific yew harvest. Here is a summary of those directions:

BLM Pacific Yew Strategy Document

BLM will publish a draft Pacific Yew Strategy Document in June, 1992. Copies will be distributed to the public for a 45-day comment period. The draft strategy addresses Pacific yew management on BLM administered lands in Oregon, Washington, Idaho, and California. It responds to Congressional direction in the 1992 Interior Appropriation Act for BLM to "develop a comprehensive strategy document for ensuring a sustainable supply of Pacific yew for the medical community with the least impact to the environment and to the Pacific yew resource." Copies of the draft strategy will be available from BLM offices in Oregon, Washington, northern Idaho and northern California.

BLM 1992 Pacific Yew Administrative Policies

Confines yew harvest to existing timber sales and dead yew trees in certain areas. Places heavy emphasis on pre-peeling bark before commercial timber operations begin. Requires yew surveys of existing and recently expired timber sales. Specifies yew utilization standards and harvesting techniques. Provides guidelines for yew sale procedures. Emphasizes measures for protecting peeled yew logs from unnecessary burning. Requires strict accountability of harvest including field weighing of bark by BLM representatives. Establishes sale prices for yew products. Provides guidance for making yew resources available to third parties, including traditional users and American Indians. Requires collection of yew data during silvicultural surveys. Directs district managers to take measures for protecting Pacific yew from theft.

Pacific Yew Bark Utilization

To: Forest Supervisors of the Olympic, Mt. Baker-Snoqualmie, Gifford Pinchot, Mt. Hood, Willamette, Umpqua, Rogue River, Siskiyou, Siuslaw, and Umatilla National Forests
From: Regional Forester, Pacific Northwest Region
January 6, 1992

The Forest Service will assume more administrative responsibility for utilization standards, most importantly when burning of the unit is planned in preparation for replanting. District personnel should review each unit after yew collection is completed and call collectors back if collection is not complete. Collectors may have to finish these units before they can enter additional units.

Pacific Yew Fuel Treatments

To: Forest Supervisors of the Pacific Northwest Region
From: Regional Forester
February 11, 1992

Burn units (after harvest and in preparation for replanting) only after yew bark has been utilized and the remaining yew trees and stumps have been protected. Do not burn

slash piles or areas until yew bark is collected. Protect remaining yew, stumps, and new growth from fire by protective measures such as pulling slash away from yew and building fire lines.

Commercial Sales — Pacific Yew
To: Regional Foresters — Pacific Northwest Region, Northern Region, and Pacific Southwest Region
From: Chief of the Forest Service
February 25, 1992

Because of the possibility that taxol may be obtained from Pacific yew heartwood, all commercial sales of Pacific yew trees on national forests will be limited to the purpose of taxol production, with the exception of a small quantity of wood for the traditional production of bows, arrows, and wood-carving products. All Pacific yew wood will be removed from all new timber sales after the bark is removed and transported to a secure location.

Priorities for Spring Yew Harvest
To: Forest Supervisors of the Pacific Northwest Region
From: Director of Timber Management
February 25, 1992

Districts will identify areas that need immediate yew harvest before scheduled burning (in preparation for replanting), or in order to harvest yew in a unit before other tree species are harvested. Districts will identify areas that need reharvest in order to meet utilization standards.

Pacific Yew Fuel Treatments
To: Forest Supervisors of the Pacific Northwest Region
From: Regional Forester
March 9, 1992

Continue to protect yew when burning units in preparation for replanting. Survey burned units to compare survival levels to the preharvest levels. Consider artificial regeneration through seedlings or rooted cuttings; both Wind River and J.Herbert Stone nurseries are ready to propagate yew for replanting on harvested units.

Pacific Yew
To: All Forest Service employees
From: Chief of Forest Service
March 9, 1992

All employees working in the Pacific yew ecosystems must be aware of the importance of the yew and take appropriate actions to ensure that the resource is effectively used. Develop a personal knowledge of the program and its benefits to society.

Interim Guidance for Harvest and Salvage of Pacific Yew
To: Forest Supervisors—Nez Perce, Clearwater, Idaho Panhandle, Kootenai, Flathead, and Lolo National Forests
From: Regional Forester, Northern Region
March 30, 1992

Directions for managing and making yew available for the national cancer effort include: list first and second priorities for yew bark harvest areas; make every effort to salvage yew bark that could be lost in site preparations and burning; harvest bark prior to logging in all new sales and where possible in existing sales; permit yew wood for taxol only (with few exceptions); salvage yew wood in new sales and where possible in existing sales; and prepare environmental analyses for projects affecting Pacific yew.

Pacific Yew Interim Conservation Guides
To: District Rangers (through Forest Supervisors)
From: Deputy Regional Forester for the Pacific Northwest Region
April 7, 1992

"The Interim Guide to the Conservation and Management of Pacific Yew," developed by a inter-regional, inter-agency technical committee will direct the management of the Pacific yew program during the upcoming peeling season and until the environmental impact statement for Pacific yew is completed.

Please Call Us

If you have issues and concerns you would like to discuss with the team preparing this EIS, please contact Sally or Susan. The team is available to meet with individuals or groups.

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Kent Tresidder, Bureau of Land Management, Oregon/Washington yew program coordinator, (503) 280-7070

Leslie Robinette, Bureau of Land Management, public affairs specialist, (503) 280-7031

Mike Ganey, U.S. Food and Drug Administration, review chemist, (301) 443-3415

What's Next?

A. Your comments on the alternatives
B. Inventory update
C. Next steps in the EIS — moving toward the draft
D. New news about yews

National Conference on Pacific Yew — Yew're Invited

What: A conference including both general and technical sessions about yew and taxol for natural resource managers, researchers, health professionals, interest groups and citizens.

Where: LaSells Stewart Center, Oregon State University, Corvallis, Oregon.

When: August 3 to 5, 1992

Why: To increase understanding of the issues involved and to promote interaction by participants.

Who: Co-sponsored by the USDI Bureau of Land Management, the USDA Forest Service Pacific Northwest Region, the USDA Forest Service Pacific Northwest Research Station, Oregon State University College of Forestry, and the National Cancer Institute.

For registration information please contact **Toni Gwin** at Oregon State University College of Forestry, **503/737-2329**. Cost is $75, plus $10 for a field trip (optional).

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You Can Comment

We invite you to comment as we prepare the environmental impact statement. How are we doing? Have we offered a fair range of alternatives? What else should we consider as we analyze the proposed alternatives for yew harvest?

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Appendix B

Monitoring

Appendix B

Monitoring

MONITORING

The following two monitoring measures are suggested as ways to better achieve harvest and regeneration goals.

1. Monitor yew regeneration on timber sale units in conjunction with other conifer regeneration surveys. Additional useful information that could be collected includes:

    a. Compare yew stump and residual survival and growth following different site preparation methods (e.g. prescribed burns, slash and pile, yarding unmerchantable timber [YUM], etc.);

    b. Determine occurrence, distribution, and associated physical and biotic habitat of natural seedlings;

    c. Compare growth and survival of planted seedlings, planted rooted cuttings, and natural seedlings; and

    d. Determine relative effectiveness of animal protection measures.

The main purpose of this monitoring measure is to identify those timber sale units where yew regeneration is not meeting the silvicultural prescription and where remedial regeneration is required. Any additional information that is gathered will increase our knowledge about stock types, optimal seed bed conditions, and animal protection, and will help us in future propagation and regeneration efforts.

2. Monitor diameter class populations and distribution before and after harvest in partial-cut and non-sale areas. This monitoring can be carried out in conjunction with pre-sale work, contract compliance monitoring, or as part of the yew harvest permit administration procedure. The post-harvest survey should be done as soon as possible after harvest in order to provide as much feedback and adjustment of methods as possible within the same field season.

The purpose of this monitoring measure is to ensure that we harvest the correct amount of trees or shrubs and that we retain the correct percentage or minimum number as required by the selected alternative. Another purpose is to compare different methods of implementation. Where yew is sparsely and unevenly distributed, removal of a percentage of trees in each diameter class,

MONITORING

The following two monitoring measures are suggested as ways to better achieve harvest and regeneration goals.

1. Monitor yew regeneration on timber sale units in conjunction with other conifer regeneration surveys. Additional useful information that could be collected includes:

   a. Compare yew stump and residual survival and growth following different site preparation methods (e.g. prescribed burns, slash and pile, yarding unmerchantable timber [YUM], etc.);

   b. Determine occurrence, distribution, and associated physical and biotic habitat of natural seedlings;

   c. Compare growth and survival of planted seedlings, planted rooted cuttings, and natural seedlings; and

   d. Determine relative effectiveness of animal protection measures.

The main purpose of this monitoring measure is to identify those timber sale units where yew regeneration is not meeting the silvicultural prescription and where remedial regeneration is required. Any additional information that is gathered will increase our knowledge about stock types, optimal seed bed conditions, and animal protection, and will help us in future propagation and regeneration efforts.

2. Monitor diameter class populations and distribution before and after harvest in partial-cut and non-sale areas. This monitoring can be carried out in conjunction with pre-sale work, contract compliance monitoring, or as part of the yew harvest permit administration procedure. The post-harvest survey should be done as soon as possible after harvest in order to provide as much feedback and adjustment of methods as possible within the same field season.

The purpose of this monitoring measure is to ensure that we harvest the correct amount of trees or shrubs and that we retain the correct percentage or minimum number as required by the selected alternative. Another purpose is to compare different methods of implementation. Where yew is sparsely and unevenly distributed, removal of a percentage of trees in each diameter class,

particularly with retention of a minimum number of trees per acre, is not easy to implement. A number of different pre-harvest inventory and marking methods will most likely be tried to find one or more that will result in accurate harvest and retention percentages while minimizing error, cost, and time. This monitoring measure allows different methods to be evaluated and compared.

Appendix C

Mitigation Measures for the Pacific Yew

Appendix C

Mitigation Measures

Mitigation Measures for Yew Harvest

This section describes a number of mitigation measures which accompany the alternatives. The mitigation measures help define each alternative by describing more specifically how the yew is to be harvested, protected, and regenerated under each alternative.

Terms to Know

"Tree form yew"— *Upright yew plants exhibiting apical dominance, usually with only one main stem. Tree form yew typically grows taller than shrub form yew, with larger diameter stem(s).*

"Shrub form yew"— *Those yew plants with a more brush-like form, having multiple, smaller diameter stems, none of which exhibit apical dominance. Shrub form yew are typically shorter than tree form yew.*

"Residual green tree reserve"— *those trees or shrubs left on a site to provide a local seed source, or for other purposes. Where silvicultural prescriptions call for retaining green trees, the inclusion of yew trees or shrubs in the green tree reserve provides a local seed source for natural regeneration.*

"Timber sale unit"— *an area within a timber sale which has a silvicultural prescription for a (1) clearcut, (2) shelterwood, or (3) seed tree harvest method. It also refers to an area that is to be cleared for road or building construction.*

"Clearcut"— *a type of harvest where an entire stand of trees is removed in one cutting operation, leading to the establishment of an even-aged stand.*

"Shelterwood Cut"— *a type of harvest method where a portion of the mature stand is retained as a source of seed and/or shelter during the period of regeneration. The mature stand is removed in two or more cuttings. The resulting stand is even-aged.*

"Seed Tree Cut"— *a type of harvest similar to a clearcut, except that a few of the better trees of the desired species are left scattered over the area to provide seed for regeneration. The resulting stand is even-aged.*

More Terms to Know

"Partial-cut sale unit"— *an area within a timber sale which has a silvicultural prescription to cut only part of a stand. Techniques which involve "partial cutting" include thinning, salvage operations, and prescriptions designed to produce an uneven-aged stand of trees.*

"Non-sale area"— *an area in a national forest or BLM district where timber sales are allowed by land use plans (but are not scheduled in the next five years) and where yew harvest is allowed.*

"Owl conservation areas"— *those areas formally designated for protection of the northern spotted owl. They provide a contiguous block of habitat to be managed and conserved for spotted owls. The blocks are placed so as to be well distributed throughout the range of the owl and spaced closely enough to facilitate dispersal of owls among them. Habitat Conservation Areas (HCAs) as described in the Final Environmental Impact Statement on Management for the Northern Spotted Owl in the National Forests, are the type of owl conservation areas being used on national forests. For BLM forest lands, conservation areas are defined as Old-Growth Emphasis Areas (OGEA), Connectivity Areas (CON), and Owl Pair Sites (OPS), as described in the preferred alternative of the BLM's draft resource management plans and Klamath Resource Area Management Plan.*

"Local management area"— *is used for Forest Service lands and refers to an area not larger than about 20,000 acres, or to "one National Forest System Watershed (fourth or fifth-order stream basin)". (Refer to Forest Service Handbook 2509.24).*

"Tree seed zones"— *are used for BLM lands and refer to the areas established by the Western Forest Tree Seed Council; they delineate areas of similar climatic and geographic conditions.*

Mitigation Measures for Alternative B

Timber Sale Units

Both Tree and Shrub Form Yew

- Where yew harvest is planned, harvest yew in the sale unit prior to the harvest of other species, to the extent that timber harvesters' health and safety will not be jeopardized. Preharvesting may be accomplished by decking yew logs in specific locations within the sale unit during logging operations.

- Consider including vigorous, undamaged yew trees or shrubs in the green tree reserves whenever possible.

- Harvest yew that is not in the residual green tree reserve.

- To facilitate sprouting, leave yew tree stumps at least 12" high. Yew shrubs should be cut to leave 12" length above the root collar; generally this can be met by cutting shrubs where the stem emerges from the duff.

- Leave bark intact on yew stumps.

- Site-specific prescriptions will identify logging systems, site preparation and fuels reduction treatments, and conifer regeneration plans with regard to yew survival and regeneration.

- Wherever possible and practical, shade yew stumps with slash or adjacent vegetation and position reserve green trees to provide shade for yew stumps and advanced yew regeneration. Shading is not necessary in all areas and is not normally required on shrub form yew; site-specific analysis may help determine how much shading is needed.

- Monitor yew regeneration until yew regeneration prescriptions have been met. Where possible, monitor yew regeneration in conjunction with conifer regeneration and other area surveys.

- If prescribed regeneration of yew has not been achieved and there is assurance that regeneration by other means is not occurring, yew will be planted as prescribed in site-specific prescriptions.

- Do not harvest yew within 75 feet (R-5, R-6, BLM) or 50 feet (R-1) slope distance from the average high-water level of a perennial stream. This requirement may be increased to meet other resource needs.

Tree Form Yew

- Do not harvest yew trees adjacent to cut units due to their importance as a seed source.

- Use one or more of the following methods to maintain or replace yew on the site at preharvest levels or, where very abundant, at a minimum of 50 yew plants per acre:

  1. Retain and protect as much of the residual yew (stumps, trees, shrubs, advanced regeneration remaining after harvest) as possible and practical from post-harvest activities such as slash piling and burning. Plan logging systems and slash disposal methods which favor the survival of residual yew plants and stumps, e.g., grapple piling or combined machine and burning methods or special burn prescriptions. Include retention of yew and yew stumps as one of the prescribed fire objectives in burning plans. Leave litter and down wood in those patches for seedling establishments;

  2. Encourage natural regeneration (from seed already present on site) by using any site preparation methods known to favor yew seed germination and establishment. Monitor occurrence and distribution of natural seedlings; and

3. Plant rooted cuttings or seedlings from on-site sources of cuttings or seed. Cuttings could be collected before harvest. Use vexar tubing or other animal protection where browsing of young yew is predicted.

Shrub Form Yew

- Harvest shrub form yew only where practical (i.e. sufficient number of stems of utilizable size).

- Consider seed source needs on and adjacent to the unit in site-specific NEPA analysis.

- Regenerate yew shrubs to maintain adequate numbers and distribution while meeting other land management objectives. Where preharvest yew density would preclude meeting other land management objectives (for example, conifer regeneration within five years), yew density may be reduced from preharvest conditions. Site-specific silvicultural prescriptions will describe desired yew densities compatible with meeting other objectives.

- Site-specific prescriptions will provide desired site conditions for natural regeneration of yew and protect concentrations of existing yew where feasible, while still meeting other management objectives. Where on-the-ground conditions preclude this, planting of yew will be prescribed.

- Site preparation treatments will be considered in the following general order of preference:

  1. No additional site preparation;

  2. Low intensity mechanical site preparation which maintains patches of undisturbed ground including yew stumps and residual yew shrubs (Grapple piling can be effective on slopes less than 35%);

  3. Slashing in lieu of burning;

Mitigation Measures Alternatives C through G2

4. Cool burning prescriptions to maintain duff on site and limit mineral soil exposure (a cool burn would retain more duff and expose 10-20% mineral soil);

5. Yarding of whole trees or unmerchantable timber (YUM) prior to burning to reduce fuel loadings, facilitate slash disposal and reduce burn intensities. Slash from yew harvest could be spot piled away from residual plants and stumps; and

6. High intensity burning will be a last resort, when other methods will not meet management objectives.

All Sites

- **Conditions for Harvesting:** In order to harvest yew in a local management area or tree seed zone, sites of 20 to 100 acres within that management area with at least an effective population size of 500 sexually mature trees (may require census numbers larger than 500) that show evidence of reproductive buds and are at least 25 feet apart. Genetic reserve areas must be established first. If there are not sufficient yew in a local management area or tree seed zone to meet the above criteria, no yew would be harvested and existing populations would be protected as much as practical from other activities, except as provided below.

Sites Where There is Insufficient Yew for Yew Harvest

- In some instances, yew may be harvested in local management areas or tree seed zones where there are not enough yew to establish a reserve area and, therefore, a yew harvest program. For example:

1. Prior to the activity, preharvest yew that is in danger of being killed by activities such as timber sales, site preparation, prescribed fire, road construction, reconstruction, administrative site-development/main-

tenance, recreation site development/maintenance, or Native American uses; and

2. Salvage yew that is inadvertently killed by management activities or by natural causes.

- Do not harvest yew that is not in danger of being killed. Protect this yew by avoiding damage to it and maintaining or providing shade whenever practical or necessary.

- If yew is killed during other activities, regenerate it to achieve the yew densities consistent with management objectives.

Sites Where There is Sufficient Yew for Yew Harvest

Both Sale and Non-sale Areas

- **Genetic Reserve Areas:** Establish genetic reserve areas of 20 to 100 acres for every 1,000-foot (BLM) or 2,000-foot (Forest Service) elevation band in each management area where yew is present in sufficient numbers. Each reserve contains an effective population of 500 sexually mature trees (may require census numbers larger than 500) that show evidence of reproductive buds and are at least 25 feet apart. Reserve areas may be located within larger reserve systems such as northern spotted owl conservation areas, designated wilderness, selected old growth areas or Research Natural Areas. BLM elevation bands were established at 1,000 feet intervals to compensate for the intermingled private lands which often are barren of reproductive yew.

- **Riparian Areas:** No yew will be harvested within 75 feet (R-5, R-6, BLM) or 50 feet (R-1) slope distance from the average high-water level of a perennial stream. This requirement may be increased to meet other resource needs.

- **Utilization of Yew Material:** Follow current Forest Service and BLM policies for utilization of yew wood, bark, and needles. These policies may differ between Forest Service regions or national forests or between BLM districts.

- **Transfer of Yew, Administration of Permits, and Theft Prevention:** Follow current Forest Service and BLM policies.

Timber Sale Units

Both Tree and Shrub Form Yew

- Where yew harvest is planned, harvest yew of utilizable size in the sale unit prior to the harvest of other species, to the extent that timber harvesters' health and safety will not be jeopardized.

- Consider including vigorous, undamaged yew trees or shrubs in the green tree reserves whenever possible.

- Harvest yew that are not in the residual green tree reserve.

- To facilitate sprouting, leave yew tree stumps at least 12" high. Yew shrubs should be cut to leave 12" length above the root collar; generally this can be met by cutting shrubs where the stem emerges from the duff.

- Leave bark intact on yew stumps.

- Site-specific prescriptions will identify logging systems, site preparation and fuels reduction treatments, and conifer regeneration plans with regard to yew survival and regeneration.

- Wherever possible and practical, shade yew stumps with slash or adjacent vegetation and position reserve green trees to provide shade for yew stumps and advanced yew regeneration. Shading is not necessary in all areas and is not normally required on shrub form yew; site-specific analysis may help determine how much shading is needed.

- Monitor yew regeneration until yew regeneration prescriptions have been met. Where possible, monitor yew regeneration in conjunction with conifer regeneration and other area surveys.

- If adequate numbers (number of yew plants that are represented in natural stands at the same successional stage on similar sites) of yew are not present, after assurance that regeneration by other means is not occurring, yew will be planted as prescribed in site-specific prescriptions.

Tree Form Yew

- Do not harvest yew trees adjacent to cut units due to their importance as a seed source.

- Use one or more of the following methods to maintain or replace yew on the site at preharvest levels or, where very abundant, at a minimum of 50 yew plants per acre:

  1. Retain and protect as much of the residual yew (stumps, trees, shrubs, advanced regeneration remaining after harvest) as possible and practical from post-harvest activities such as slash piling and burning. Plan logging systems and slash disposal methods which favor the survival of residual yew plants and stumps, e.g., grapple piling or combined ma-

chine and burning methods or special burn prescriptions. Include retention of yew and yew stumps as one of the prescribed fire objectives in burning plans. Leave litter and down wood in those patches for seedling establishments;

2. Encourage natural regeneration (from seed already present on site) by using any site preparation methods known to favor yew seed germination and establishment. Monitor occurrence and distribution of natural seedlings; and

3. Plant rooted cuttings or seedlings from on-site sources of cuttings or seed. Cuttings could be collected before harvest. Use vexar tubing or other animal protection where browsing of young yew is predicted.

Shrub Form Yew

- Harvest shrub form yew only where practical (i.e. sufficient number of utilizable size).

- Consider seed source needs on or adjacent to the unit in site-specific NEPA analysis.

- Regenerate yew shrubs to maintain adequate numbers and distribution while meeting other land management objectives. Where preharvest yew density would preclude meeting other land management objectives (for example, conifer regeneration within five years), yew density may be reduced from preharvest conditions. Site-specific silvicultural prescriptions will describe desired yew densities compatible with meeting other objectives.

- Site-specific prescriptions will provide desired site conditions for natural regeneration of yew and protect concentrations of existing yew where feasible, while still meeting other management objectives. Where on-the-ground conditions preclude this, planting of yew will be prescribed.

- Site preparation treatments will be considered in the following general order of preference:

    1. No additional site preparation;

    2. Low intensity mechanical site preparation which maintains patches of undisturbed ground including yew stumps and residual yew shrubs (Grapple piling can be effective on slopes less than 35%);

    3. Slashing in lieu of burning;

    4. Cool burning prescriptions to maintain duff on site and limit mineral soil exposure (a cool burn would retain more duff and expose 10-20% mineral soil);

    5. Yarding of whole trees or unmerchantable timber (YUM) prior to burning to reduce fuel loadings, facilitate slash disposal and reduce burn intensities. Slash from yew harvest could be spot piled away from residual plants and stumps; and

    6. High intensity burning will be a last resort, when other methods will not meet management objectives.

Partial-Cut Units/Non-sale Areas

Both Tree and Shrub Form Yew

- **Prioritization of Harvest Areas:** In areas where no clearcut, shelterwood, or seed tree timber sales are planned, stands containing yew will be prioritized for yew harvest. Stand priority order will vary from area to area. Low priority stands will be harvested for yew last; these stands will be stands that are valued for certain extraordinary characteristics (such as old-growth, wildlife habitat, unique yew scarcity/abundance). High priority stands are stands that are less extraordinary for the above values and will be harvested for yew first.

- **Percent of Harvest and Leave Trees or Shrubs:** The alternatives call for different maximum percentages of yew harvest in each stand, as well as different minimum numbers of unharvested yew trees per acre (TPA) for each of three diameter classes: (For shrub form, there are no diameter classes)

Alternative	Maximum Percent Harvest	Minimum TPA Not Harvested
A	0	NA
B	100	no minimum
C	25	5
D	50	5
F	75	2
G1	50	no minimum
G2	50	no minimum (5 in OCAs)

- **Fire Hazard Reduction:** Where fire risk due to yew harvest is high, decrease risk by one or more of the following measures: treat yew slash; identify potential fire-hazardous conditions and activities and develop guidelines to reduce or eliminate them in site-specific prescriptions; control human access to woods by regulating the number of people and time of entry; and when fire danger is high, prohibit use of machinery and use instead handtools, horses, etc.

Tree Form Yew

- Leave unharvested yew trees distributed through the stand to reflect the natural distribution in each of three diameter classes (< 11", 11 - 20", > 20" stump diameter).

- In any one harvest area, either cut the whole yew tree for bark, wood, or needle production or remove up to half of the foliage for foliage-only production.

- For whole yew tree harvest, leave at least a 12" high stump, with the bark intact; shade the yew stump with slash or adjacent vegetation wherever possible or necessary; do not re-enter the stand to harvest whole yew trees for at least ten years.

- For foliage harvest, remove half of the foliage evenly throughout the crown from yew greater than 1" DBH (diameter at breast height); do not remove foliage from yew with less than 1" DBH; re-enter the stand only after foliage re-growth has occurred; re-harvest foliage from the same trees each time.

Shrub Form Yew

- In any one harvest area, cut either the whole shrub for bark or needle production or remove half the foliage for foliage-only production.

- Retain at least 75, 50, or 25 percent (depending on alternative) of the shrub cover by one of the following methods:

  1. Harvest shrubs from no more than 75, 50, or 25 percent of the unit. Site-specific prescriptions will decide whether distribution of unharvested area is by strip, block or individual shrub harvesting method;

  2. Harvest single shrub or group of shrubs; and

  3. Harvest all merchantable stems where there is at least 75, 50, or 25 percent cover provided by remaining unmerchantable stems.

- For whole shrub harvest, leave a stump length of 12" from the root collar, with bark intact; do not cut yew shrubs less than 1" diameter (the diameter is measured where the stem emerges from the duff); do not re-enter the stand to harvest whole shrubs for at least 10 years.

- For foliage harvest from shrubs, remove no more than half of the foliage, evenly distributed throughout the crown, from yew with diameters over 1" (the diameter is measured where the stem emerges from the duff); do not remove foliage from yew that is less than 1" diameter; do not reenter the stand to harvest foliage for at least five years.

Special Area Mitigation Measures

Mitigation Measures for Yew Harvest in Owl Conservation Areas for Alternative G2

- **Conservation Areas:** Conservation areas are defined here as Habitat Conservation Areas (HCA) for national forest land, as defined by the Final EIS on Management for the Northern Spotted Owl (1992). For BLM forest lands, conservation areas are defined as Old-Growth Emphasis Areas (OGEA), Connectivity Areas (CON), and Owl Pair Sites (OPS), as described in the preferred alternative of the BLM's draft resource management plans and Klamath Resource Area Management Plan.

- On Forest Service lands, harvest yew only in Category 1 HCA's that have more than 15 pairs or resident singles and Category 2 HCA's that have occupancy greater than 75% of the future adjusted occupancy target. On BLM lands, harvest yew only in Non-Deferred OGEAs and CON areas. There are four categories of HCA's:

  Category 1 - blocks of habitat to support at least 20 pairs.
  Category 2 - blocks of habitat to support 2 to 19 pairs.
  Category 3 - blocks of habitat to support individual pairs.
  Category 4 - blocks of habitat that may be smaller than the median annual home-range size but provide connectivity or potential habitat for future nest sites.

- On Forest Service lands, harvest yew only after the HCA has been inventoried following current protocol. On BLM lands, harvest yew only after project areas have been surveyed according to standard BLM Northern spotted owl survey procedures.

- Do not harvest yew within 0.5 mile radius (500 acres) of known spotted owl nest sites or activity centers on Forest Service lands. For BLM lands, do not harvest yew in the 100 acres surrounding known nest sites or activity centers.

- Harvest yew according to the Partial-cut Units/Non-sale Areas guidelines, found within the Mitigation Measures for Alternatives C through G2. In each of the three diameter classes (< 11", 11 - 20", > 20" stump diameter), harvest no more than 50% of the yew in each area while retaining at least 50% of the yew or five yew trees per acre (whichever is greater).

Mitigation Measures for Yew Harvest in Moose Winter Range for Alternatives B through G2

Designated Lands for Moose Winter Range on the Nez Perce National Forest: Moose winter range is managed for its Pacific yew component on the Nez Perce National Forest in north-central Idaho. The Nez Perce Forest Plan identifies 63,000 acres as Management Area #21 (MA21). The stated goal for MA21 is to "Manage the grand fir-Pacific yew plant communities to provide for a continuing presence of Pacific yew "suitable" for moose winter habitat."

Optimum Conditions: Limited research suggests that stands which have optimum conditions for the yew component of moose winter range have 50% cover of large overstory trees (at least 40 feet tall and usually over 90 years old) and at least 30 percent cover of tree-form yew. Suggested minimum size for land units to be managed for winter range is 1,000 acres. Riparian areas, ridgetops, and benches are the most frequently used topographic areas. Key winter range characteristics related to Pacific yew include thermal cover and browse availability. Some other characteristics include topographic site, elevation and slope.

On areas of the Forest where site-specific NEPA analysis has been completed, stands have been validated as MA21. The Nez Perce National Forest is in the process of refining the standards for MA21 based upon Forest-wide inventory data collected during the 1992 field season. With the new inventory data, many more MA21 stands will be confirmed.

Follow the mitigation measures for Alternatives C through G2. Exceptions are noted below.

All Sites

- Meet the mitigation measures for Management Area 21 of the Nez Perce National Forest Plan. Harvest Pacific yew only where the suitability as moose winter habitat is maintained.

Timber Sale Units

- Follow the Timber Sale Unit portion of the Mitigation Measures for Alternatives C through G2, except leave 50% of the original preharvest yew in patches or other patterns that can be protected from logging damage or site preparation activities.

Partial-Cut Timber Sale Units

- Follow the Partial-cut Units/Non-sale Area portion of the Mitigation Measures for Alternatives C through G2, at the 50% harvest level.

- Leave either 50% of the yew trees or five yew trees per acre (whichever is greater) distributed across the stand to reflect ecological needs for each of three yew size classes (< 11", 11 - 20", > 20" stump diameter).

Non-sale Areas

- Follow the Partial-cut Units/Non-sale Area portion of the Mitigation Measures for Alternatives C through G2, except for determining the harvest level.

- The interdisciplinary team conducting the site-specific analysis will include a wildlife biologist. Yew harvest will consider snow interception and browse availability, as well as providing yew products. Actual harvest levels will be recommended during site-specific analysis.

- Leave a minimum of either 50% of the yew trees or five yew trees per acre (whichever is greater) evenly distributed through the stand for each of three yew size classes (< 11", 11 - 20", > 20", stump diameter).

- Harvest a maximum of 50% of the yew in the stand; either cut the whole tree or remove one-half of the foliage.

Mitigation Measures for Yew Harvest in Port-Orford-cedar Areas for Alternatives B - G2

Management of Pacific yew in areas within the natural range of Port-Orford-cedar (POC) will follow the same analysis processes developed for management of POC root disease. The standards, guidelines, or mitigation measures to use are determined by using the following process to analyze the risk inherent in various management activities.

Steps in the Port-Orford-cedar Analysis Process:

1. Management direction for Port-Orford-cedar;
2. Project description;
3. Management objectives by subunit;
4. Risk assessment - matrix and narrative;
5. Disease control measures - listing and cost analysis;
6. Potential impact - analysis and narrative;
7. Monitoring;
8. Public involvement; and
9. Maps.

1. **Management Direction for Port-Orford-cedar:** USDA Forest Service Region Five/Region Six Port-Orford-cedar Root Disease Action Plan - June 29, 1988. This is a formal commitment by both regional foresters for (1) Inventory and Monitoring, (2) Research, (3) Public Involvement and Edu-

cation, and (4) Management Policy. In short, this commitment provides the support to ensure the viability and continued presence of Port-Orford-cedar in the ecosystem throughout its native range on Forest Service managed lands.

- List forest plan standards and guidelines related to Port-Orford-cedar.

- List project-level direction relating to Port-Orford-cedar (special management area concerns, issues with the Proposed Action of the project, etc.).

2. **Description of Project:** Brief description of project (acres, number of units, haul route, and activities with risk of spreading disease).

3. **Management Objectives by Subunit:** Delineate subunits that have similar management objectives based on current disease status. A subunit may be a drainage, an area behind a gate, a road segment, a group of timber harvest units, or any other logical delineation. A subunit may have more than one objective (see examples B and C). Post-activity monitoring will decide on success of control strategies in meeting objectives of each subunit.

Objective

A Prevent the **import** of disease into uninfected areas (off-site spores picked up and carried into uninfected project area).

B Prevent the **export** of disease to uninfected areas (on-site spores moved to off-site uninfected area).

C Minimize the rate of spread in areas where the disease is endemic or infection is intermittent.

4. Risk Assessment Matrix and Narrative:

Percent POC (IMPACT)	Proximity of POC to Roads (Hazard)		
	Low >500 ft. below > 50 ft. above	**Moderate** >100-500 ft. below > 50 ft. above	**High** <100 ft. below < 50 ft. above
Low (1-5%)	Low Risk	Low Risk	Moderate Risk
Moderate (5-20%)	Low Risk	Moderate Risk	High Risk
High (>20%)	Moderate Risk	High Risk	High Risk

Select a risk level for the whole project and each subunit, and describe your reasons. Considerations should include: large uninfested drainages with high priority for disease protection; water use away from roads; increased access by non-project activities; number of soil-disturbing activities scheduled; distance to nearest infection source; and roadside POC with disease immediately downstream.

Projects or subunits with HIGH risk should have disease control measures applied and/or may trigger the need for notification of key people who might have technical knowledge that would be helpful in the analysis process. Projects or subunits with MODERATE or LOW risk may have few or no disease control measures applied, based on site-specific concerns.

5. **Disease Control Measures:** Select disease control strategies below that meet management objectives. Modify the wording as needed to fit a given situation and list the subunits to which this prescriptive element applies. An option would be to have a list of control strategies for each subunit. Delete those strategies which do not apply.

Engineering and Road Management (E):

E-1 Road locations should be made, when possible, below cedar areas or on opposite sides of ridges.

E-2 Control drainage from roads so that it is concentrated into existing stream channels when possible.

E-3 Locate and design waste areas so they do not spread infection spores.

E-4 Limit road construction/maintenance and associated slash disposal to the dry season.

E-5 Machinery and vehicles working and traveling on road need to be washed before entering project areas.

E-6 Wash equipment before leaving infected areas.

E-7 Close roads with guardrails, gates, physical blockades, or "putting to bed." Restrict product utilization and management activities to the dry season (June 1 through September 30). Maintenance and enforcement is included.

E-8 Avoid use of potentially infected water (for such projects as dust abatement, compaction, excavation, seeding, fire suppression, etc.) or treat water with chlorine.

E-9 Where conditions permit, establish and maintain an insloped road template and site-specific berms on the outside edges of roads to prevent downslope flow of contaminated water.

E-10 Establish road rules to prevent timber haul during periods when spores will be spread widely.

E-11 Access to the project area will be along routes with least occurrence of infection sites.

E-12 Pave or add uninfected rock to raise roadbed a minimum of 12 inches, to length of 50 feet before and after infection site.

E-13 When compaction water creates adverse wet conditions in high-sensitivity areas, water rock at the rock pit or other agreed-to sites prior to hauling to the construction area.

E-14 Use of surfacing materials appropriate for dry-weather haul (i.e., pit-run grid-rolled rock, sandstone, oil, lignin, pavement). Avoid creation of wet road conditions in high-sensitivity areas. The alternative is to require dry haul on dirt surfacing - rip, seed, and close road.

Timber Harvest (T):

T-1 Limit the operating season of timber sale operations to the drier months (June 1 to September 30) <u>and</u> discontinue operations during periods of rain or wet weather.

T-2 Harvest the units in priority order to minimize the spread of spores to uninfected areas. Infected units may be harvested after uninfected units.

T-3 When feasible, plan downhill logging to avoid road construction above an uninfected stand.

T-4 Use helicopter logging to protect high value cedar stands.

T-5 Use service contracts to harvest timber with more control of activities.

T-6 Wash logging trucks and other equipment when moving from infected to uninfected areas or subdivisions.

T-7 Wash logging equipment prior to entering sale areas.

Stand Management (S):

S-1 Identify low risk areas and emphasize maintaining and/or introducing Port-Orford-cedar into the species mix.

S-2 Plant POC singly at 25 ft. spacing or in groups of 10-20 trees at 100 ft. spacing, independent of other stocking.

S-3 Avoid planting POC within 50 feet of roads, streams or wet areas.

S-4 During precommercial thinning (PCT) thin POC at a 25 foot spacing, independent of other crop trees, or space POC in groups 100 feet apart where possible.

S-5 As part of PCT, remove POC from areas adjacent to roads, streams and other high risk areas.

S-6 To ensure the presence of POC through the rotation, leave thrifty cedar during commercial thinning.

S-7 Manage the cedar component of the stand on a longer rotation than the other associated conifers. Example: Carry cedar through two or three fir rotations.

S-8 Plant container-grown POC until bare root stock can be certified disease free at the Nursery.

S-9 Indicate in stand records [GIS, etc.] that POC protection measures have been implemented.

S-10 Minimize management entries during wet weather. Wash vehicles when such entries are made. Associated with formal road closure. Maintain consistency with requirements of sale purchasers, public.

S-11 Where possible, coordinate prevention/control activities with adjacent private landowners.

S-12 Remove/sanitize POC from high risk portion of road sides. Accomplish work during the dry season between June 1 and September 30.

S-13 Post-activity monitoring (biannual field monitoring check-list; annual monitoring report due December 1st).

Other (O):

O-1 Administrative closure orders. (CFR CLOSURE; SIGN PLAN)

O-2 Coordinate other products utilization with POC control needs and road closures. Examples: fuelwood cutting, cedar bough cutting.

O-3 Avoid using potentially infected water sources for fire suppression, or treat water with chlorine (12 fl.oz./1000 gallons).

Disease Control Cost/Effectiveness Estimate			
	Net Estimated Effectiveness	Direct FS Cost*	Indirect User Cost
Net Effect - All Treatments	High	High	Medium
Monitoring Requirements: Drive and walk-through inspections associated with this project.		Medium	
*Cost Definitions: Low = <$1,000 Medium = $1,000-$10,000 High = >$10,000			

6. **Potential Impact Analysis:** This section is to provide a more thorough analysis of the potential impact of the project after considering prescribed control measures. Assess the potential indirect and cumulative effects of the planned activity. Consider the beneficial and/or uncertain effects of the mitigation measures prescribed above for both onsite and offsite/downstream stands. This task should include the interdisciplinary team for the purpose of estimating impacts to other resources.

a. Following mitigation, is *P.lateralis* likely to infect a major amount of the analysis area? [Ref. CEQ Reg. 1508.27] If NO, then no secondary or cumulative effect. If YES, continue. (YES/NO). (Major amount of the analysis area refers to (1) great or large in relative importance to POC existence in the near proximity and over its range, (2) notable or conspicuous in effect or scope (e.g., visually detracting), or (3) posing a serious risk to the ecosystem, its neighbor POC and the total population.);

b. Will the potential secondary and cumulative effects cause meaningful levels of mortality? (YES/NO) Explain decision in narrative. (Meaningful levels of mortality is a mortality rate of 25 percent of existing Port-Orford-cedar over the next 20 year period.); and

c. Write a potential impact narrative to document the basis for each decision on the previous questions.

7. **Monitoring:** Refer to the POC monitoring plan and list here the subunits that need to be monitored and when. Include specific locations of concern, such as roads, harvest units, drainages, etc. Post-activity monitoring will decide on success of control measures in meeting management objectives for each subunit.

8. **Public Involvement:** Briefly describe how you have incorporated public involvement in the disease control strategy (scoping, field visits, etc.).

Control Strategy Prepared By: ____________________

Approved By: (As appropriate) ____________________

9. **Port-Orford-cedar Analysis Map:** This map should show all details of the project which allow the reader to fully understand the prescription. The infection status of each road, harvest unit, etc. should be displayed.

Appendix D

Land Ownerships

Appendix D

Land Ownerships

Introduction

The following tables and maps provide information on administrative units within the native range of the Pacific yew. The tables and maps are based on interpretation of the Pacific Yew Native Range Map 86W and 86N in Little, March, 1971; "Atlas of U.S. Trees, Vol. 1, Conifers and Important Hardwoods, USDA-Forest Service; Misc. Publication 1146; by Elbert L. Little, Jr.

***Table D-1:** USDA-Forest Service-Administered Lands in the Native Range of Pacific Yew*

State	National Forest	Wildernesses and National Monuments	
Washington	Olympic	Buckhorn	The Brothers
		Colonel Bob	Wonder Mountain
		Mount Skokomish	
	Mount Baker-Snoqualmie	Mount Baker	Henry M. Jackson
		Glacier Peak	Alpine Lakes
		Noisy-Diobsud	Clearwater
		Boulder River	Norse Peak
	Gifford Pinchot	William O. Douglas	Indian Heaven
		Goat Rocks	Trapper Creek
		Glacier View	Mount St. Helens National Monument
		Tatoosh	
		Mount Adams	
	Colville	Salmo-Priest	
	Wenatchee	Glacier Peak	Lake Chelan-Sawtooth
		Henry M. Jackson	William O. Douglas
		Alpine Lakes	Goat Rocks
		Norse Peak	
	Umatilla (WA)	Wenaha-Tucannon	
Note: The Columbia Gorge National Scenic Area, which lies in both Washington and Oregon, is a national forest-level administrative unit.			

Table D-1: USDA-Forest Service-Administered Lands in the Native Range of Pacific Yew (continued)

State	National Forest	Wildernesses and National Monuments	
Oregon	Mount Hood	Mount Jefferson	Columbia
		Mount Hood	Bull of the Woods
		Badger Creek	Salmon-Huckleberry
	Siuslaw	Cummins Creek	Rock Creek
		Drift Creek	
	Willamette	Mount Jefferson	Bull of the Woods
		Mount Washington	Middle Santiam
		Three Sisters	Menagerie
		Diamond Peak	Waldo Lake
	Deschutes	Mount Jefferson	Diamond Peak
		Mount Washington	Mount Thielson
		Three Sisters	
	Umpqua	Mount Thielsen	Boulder Creek
		Rogue-Umpqua Divide	
	Winema	Mount Thielsen	Mountain Lakes
		Sky Lakes	
	Siskiyou	Grassy Knob	Siskiyou
		Kalmiopsis	Wild Rogue
		Red Buttes	
	Rogue River	Sky Lakes	Rogue-Umpqua Divide
		Red Buttes	
	Umatilla (OR)	North Fork Umatilla	North Fork John Day
	Wallowa-Whitman	Monument Rock	Eagle Cap
		North Fork John Day	Hells Canyon

Note: The Columbia Gorge National Scenic Area, which lies in both Washington and Oregon, is a national forest-level administrative unit.

Table D-1: USDA-Forest Service-Administered Lands in the Native Range of Pacific Yew (continued)

State	National Forest	Wildernesses and National Monuments	
Northern California	Klamath	Red Buttes Siskiyou Marble Mountain	Russian Trinity Alps
	Six Rivers	Siskiyou Trinity Alps	North Fork Yolla Bolly-Middle Eel
	Shasta-Trinity	Mount Shasta Castle Crags	Chanchelulla
	Mendocino	Snow Mountain	Yolla Bolly-Middle Eel
	Lassen	Thousand Lakes Caribou	Ishi
	Plumas	Bucks Lake	
	Tahoe	Granite Chief	
	Eldorado	Desolation	Mokelumne
Northern Idaho	Idaho Panhandle	Salmo Priest	
	Clearwater	Selway-Bitterroot	
	Nez Perce	Selway-Bitterroot Gospel Hump Hells Canyon	Frank Church-River of No Return
	Bitterroot	Selway-Bitterroot	
Western Montana	Kootenai	Cabinet Mountains	
	Flathead	Great Bear Bob Marshall	Mission Mountains
	Lolo	NA	

Table D-2: USDI-Bureau of Land Management-Administered Lands in the Native Range of Pacific Yew

State	Districts	Resource Areas	
Washington	Spokane	Wenatchee	Border
Oregon	Salem	Tillamook Yamhill Clackamas	Alsea Santiam
	Eugene	Coast Range McKenzie	South Valley
	Roseburg	Drain North Umpqua	South Umpqua Dillard
	Coos Bay	Umpqua Tioga	Myrtlewood
	Medford	Glendale Butte Falls	Grants Pass Ashland
	Prineville	Deschutes	Central Oregon
	Lakeview	Klamath Falls	
	Vale	Baker	
Northern California	Ukiah	Arcata	Redding
	Susanville	Susanville	
	Bakersfield	Sacramento	
Northern Idaho	Coeur D'Alene	Cottonwood	Emerald Empire
Western Montana	N/A		

Table D-3: USDI-National Park Service-Administered Lands in the Native Range of Pacific Yew

State	National Park
Washington	North Cascades Mount Rainier Olympic
Oregon	Crater Lake
Northern California	Lassen Volcanic Redwood
Northern Idaho	N/A
Western Montana	N/A

Table D-4: USDI-Bureau of Indian Affairs-Administered Lands in the Native Range of Pacific

State	American Indian Trust Lands		
Washington	West of Cascade Range		East of C. R.
	Nooksack Lummi Upper Skagit Swinomish Stillaguamish Sauk-Suiattle Tulalip Makah Quileute Hoh Quinault	Lower Elwha Ozette (Jamestown Klallam) Port Gamble Port Madison Skokomish Squaxin Island Puyallup Muckleshoot Nisqually Chehalis Shoalwater Bay	Yakima Colville Spokane Kalispel
Oregon	West of Cascade Range		East of C. R.
	Grand Ronde Siletz Coos, Lower Umpqua, and Siuslaw	Cow Creek Band of Umpqua Klamath	Warm Springs Umatilla
Washington	West of Cascade Range		East of C. R.
	Nooksack Lummi Upper Skagit Swinomish Stillaguamish Sauk-Suiattle Tulalip Makah Quileute Hoh Quinault	Lower Elwha Ozette (Jamestown Klallam) Port Gamble Port Madison Skokomish Squaxin Island Puyallup Muckleshoot Nisqually Chehalis Shoalwater Bay	Yakima Colville Spokane Kalispel
Northern California	West of Interstate 5 (I-5)		East of I-5
	Smith River Karok Resighini Yurok Big Lagoon Trinidad Hoopa Valley Blue Lake Round Valley Laytonville	Sherwood Valley Redwood Valley Coyote Valley Pinoleville Upper Lake Robinson Sulphur Bank Hopland Big Valley	Lookout Big Bend Roaring Creek Montgomery Cr. Susanville Greenville Enterprise Berry Creek
Northern Idaho	Kootenai	Coeur D'Alene	Nez Perce
Western Montana	Flathead		

Table D-5: Lands in Other Ownerships in the Native Range of Pacific Yew

State	County			
Washington	**West of Cascade Range**		**East of C. R.**	
	Whatcom	Mason	Klickitat	
	San Juan	Thurston	**Northwest Area**	
	Skagit	Pierce	Ferry	
	Island	Lewis	Stevens	
	Snohomish	Pacific	Pend Oreille	
	King	Wahkiakum	Spokane	
	Clallam	Cowlitz	**Southeast Area**	
	Jefferson	Skamania	Columbia	
	Kitsap	Clark	Garfield	
	Grays Harbor		Asotin	
Oregon	**West of Cascade Range**		**East of C. R.**	
	Clatsop	Marion	Hood River	
	Columbia	Linn	Wasco	
	Tillamook	Benton	Jefferson	
	Washington	Lane	Klamath	
	Multnomah	Douglas	**Northeast Area**	
	Yamhill	Coos	Umatilla	
	Clackamas	Curry	Union	
	Lincoln	Josephine	Wallowa	
	Polk	Jackson		
Northern California	**Northwest Area**		**Northeast Area**	
	Del Norte	Tehama	Lassen	Nevada
	Siskiyou	Mendocino	Plumas	Placer
	Humbolt	Glenn	Butte	Eldorado
	Trinity	Lake	Yuba	Amador
	Shasta	Colusa	Sierra	
Northern Idaho	Boundary	Latah		
	Bonner	Idaho		
	Kootenai	Lewis		
	Shoshone	Nez Perce		
	Clearwater			
	Benewah			
Western Montana	**Northwest Area**			
	Lincoln	Mineral		
	Sanders	Missoula		
	Flathead	Powell		
	Lake			

Figure D-1: *Pacific Yew Native Range (Washington)*

Figure D-2: Pacific Yew Native Range (Oregon)

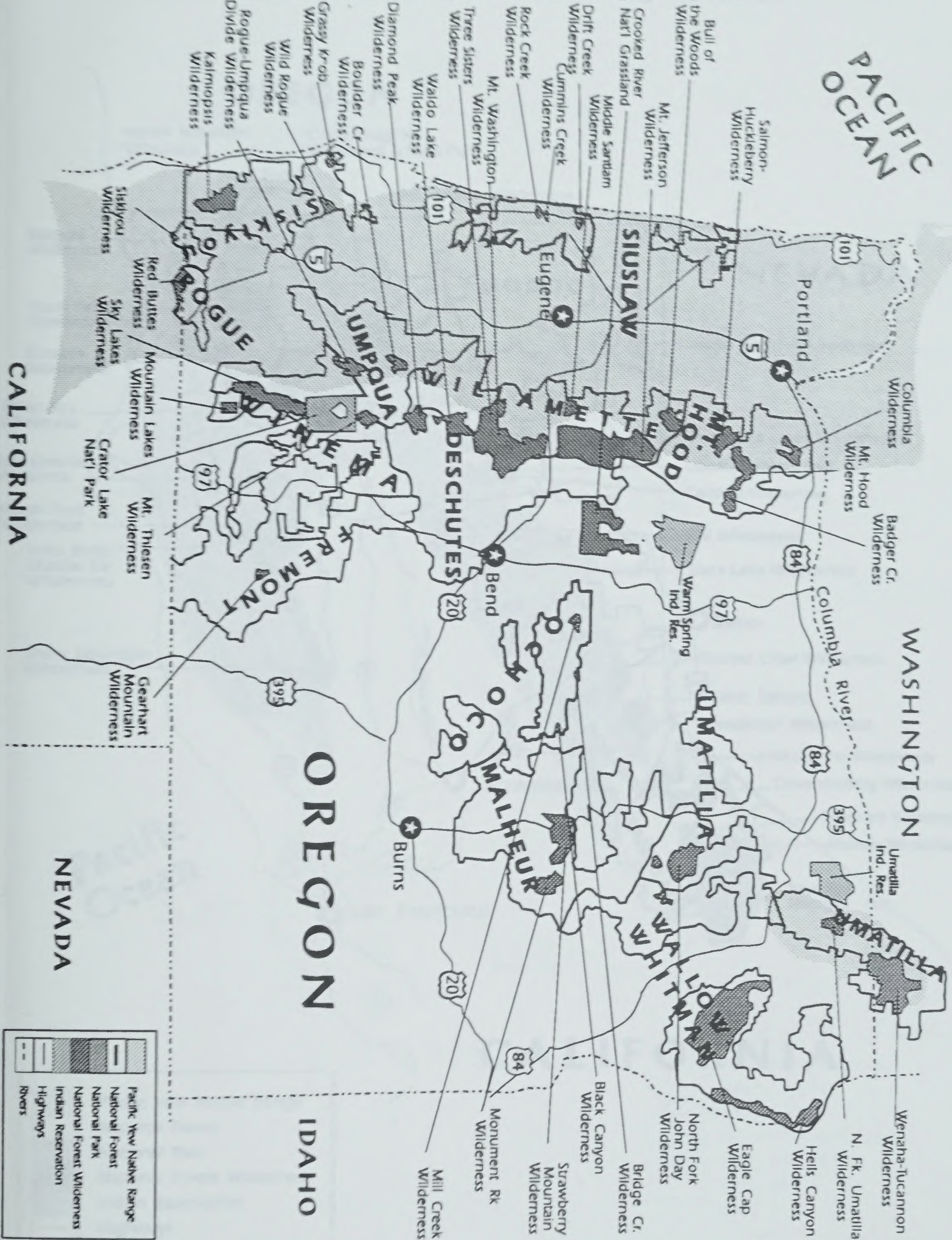


Figure D-3: Pacific Yew Native Range (California)

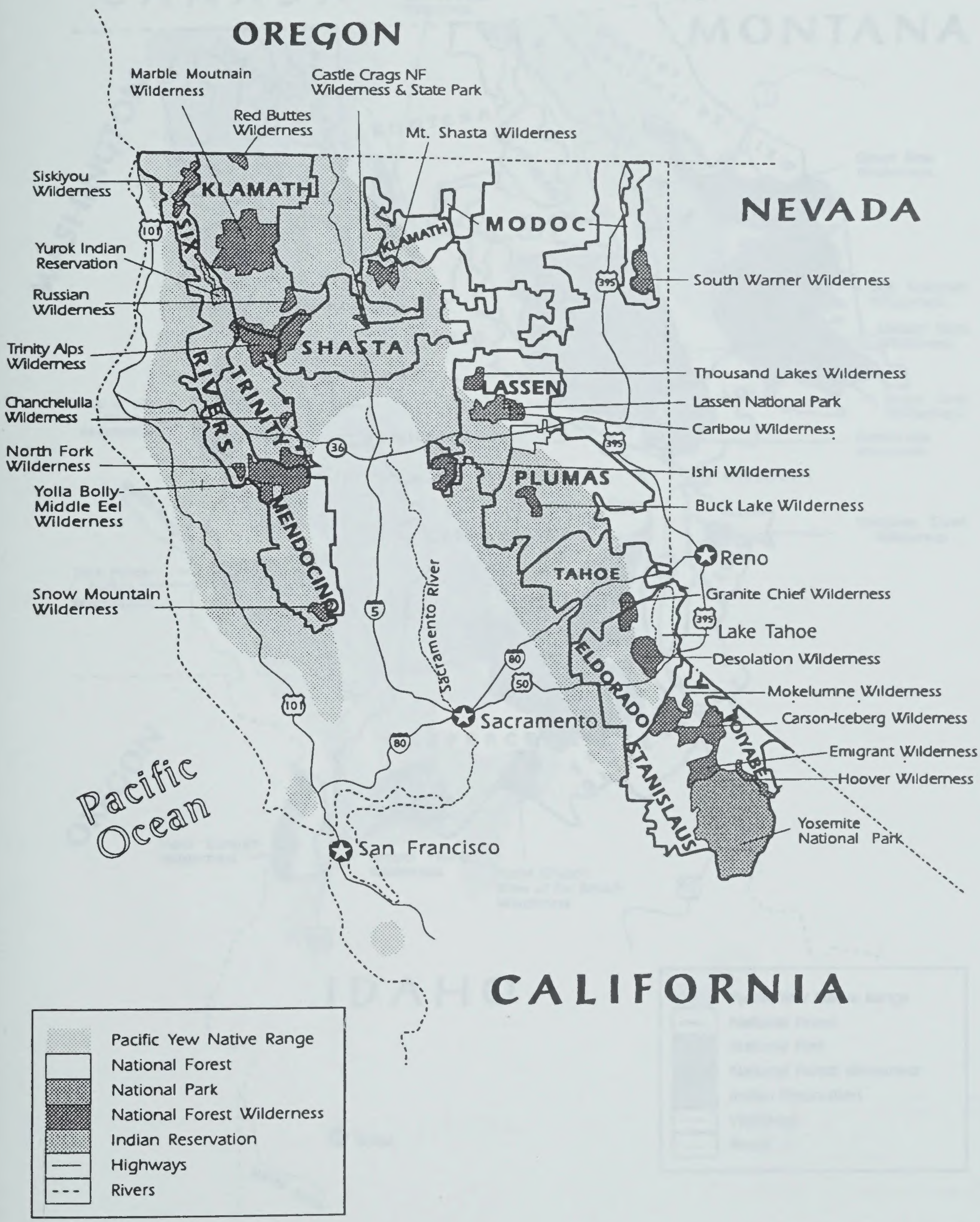


Figure D-4: *Pacific Yew Native Range (Northern Idaho and Western Montana)*

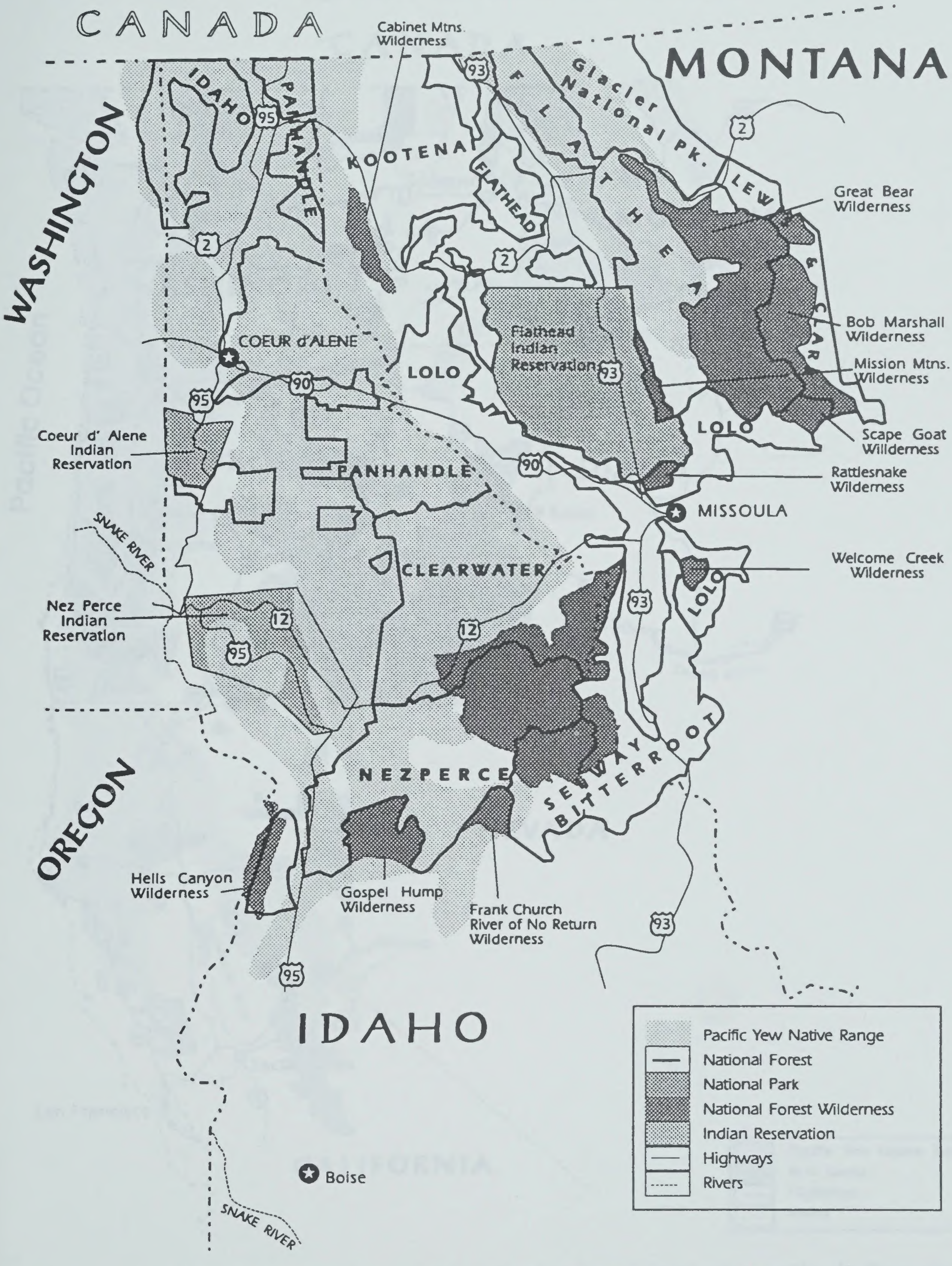
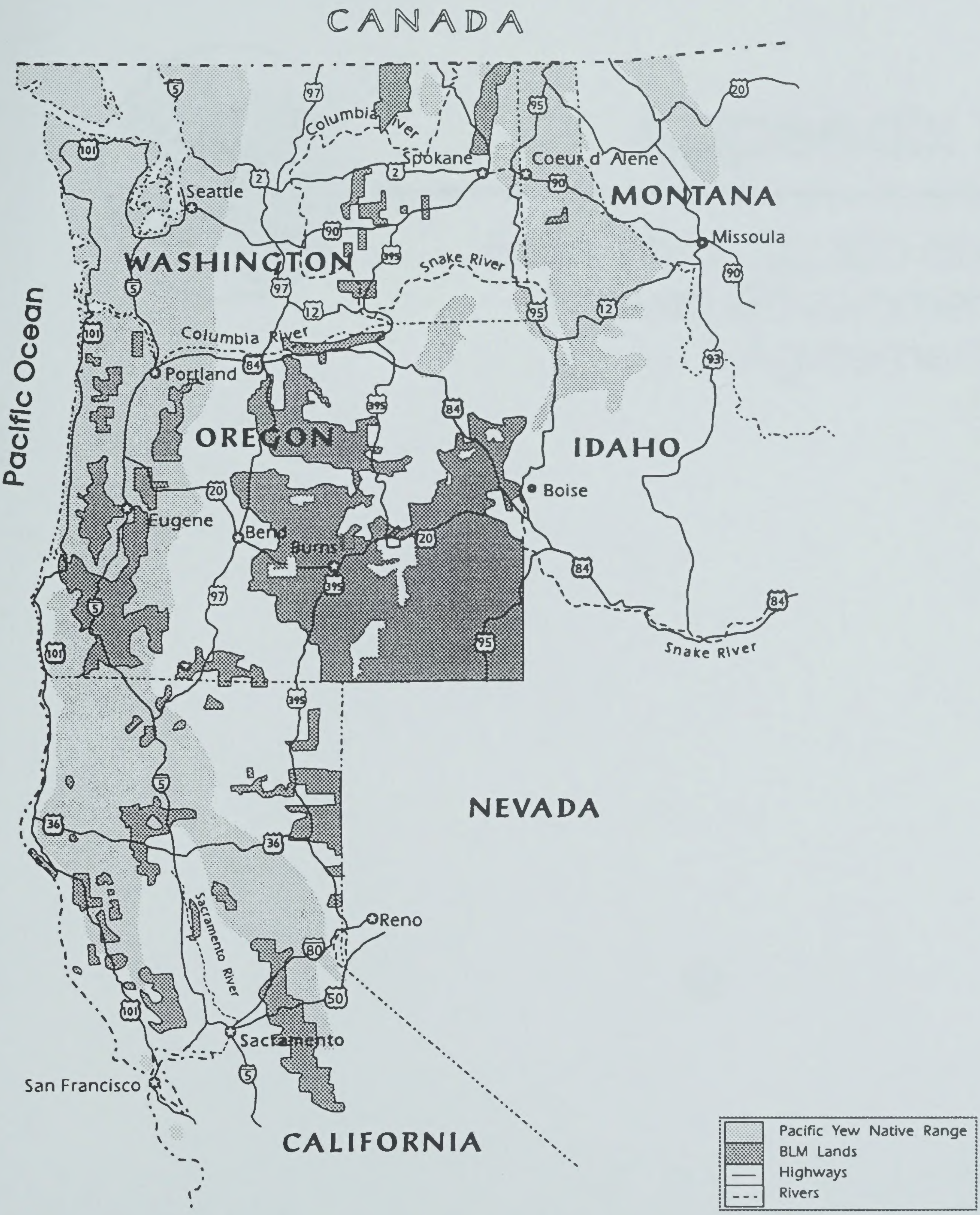


Figure D-5: *Pacific Yew Native Range within Bureau of Land Mangement Lands*(Washington, Oregon, California, Idaho, Western Montana)*



**Major blocks of land represented, most of their land occurs in every other section in the major block of land).*

Appendix E

Bristol-Myers Squibb and Federal Government Agreements

Appendix E

Bristol-Myers Squibb and Federal Government Agreements

E Agreements

Introduction

This appendix is a compilation of the agreements forming the basis of the Pacific yew harvest program on Federal lands. In order of appearance it contains the following:

COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT FOR THE CLINICAL DEVELOPMENT OF TAXOL

WHEREAS taxol, an investigational new drug derived from the bark of *Taxus brevifolia* ("*taxus*"), the Pacific Yew tree, has demonstrated promising antitumor activity in pre-clinical testing and clinical trials; and

WHEREAS the Division of Cancer Treatment, National Cancer Institute ("NCI") has conducted pre-clinical testing and clinical trials of taxol and is seeking to enter into a collaborative research and development agreement ("CRADA") with a pharmaceutical company which has the facilities, experience and expertise necessary to develop taxol into an approved drug available to the public; and

WHEREAS NCI has determined, after reviewing the response to its invitation for CRADA development published in the Federal Register on August 1, 1989, that Bristol-Myers Squibb Company ("Bristol-Myers Squibb") is a pharmaceutical company that meets the published criteria for entering into a taxol CRADA; and

WHEREAS NCI and Bristol-Myers Squibb (the "Parties") wish to collaborate in research on, and the development of, taxol as an antitumor agent, and to generate data necessary to obtain

approval from the Food and Drug Administration ("FDA") to market taxol;

NOW THEREFORE, in consideration of the promises and undertakings described herein, NCI and Bristol-Myers Squibb agree as follows:

1. JOINT STEERING COMMITTEE

A. Promptly upon the execution of this CRADA, NCI and Bristol-Myers Squibb shall form a Joint Steering Committee (the "Steering Committee"). The Steering Committee will be responsible for the design, implementation, oversight and evaluation of clinical research and development subject to this CRADA; for determining the scope and magnitude of clinical trials necessary to explore taxol's clinical utility; for establishing the order and priority of clinical trials; and for other taxol clinical research and development activities under this CRADA as otherwise agreed to by the Steering Committee.

B. NCI and Bristol-Myers Squibb shall have equal voice in decisions of the Steering Committee. The initial composition of the Steering Committee shall be five voting members on behalf of NCI and five voting members on behalf of Bristol-Myers Squibb. A Steering Committee member representing Bristol-Myers Squibb will chair the Steering Committee. The membership of the Steering Committee may be changed from time to time as mutually agreed by NCI and Bristol-Myers Squibb.

C. In the event agreement cannot be reached by the Steering Committee on an issue subject to this CRADA, the matter shall be referred to, and a decision will be made jointly by, Dr. Steven Carter of Bristol-Myers Squibb, and Dr. Bruce Chabner of NCI.

D. If the persons identified in Subparagraph C of Paragraph 1 are unable to resolve a dispute within thirty (30) days after referral from the Steering Committee, the Director National Institutes of Health shall propose a resolution. Nothing in this Paragraph shall preclude the Parties from pursuing any and all available administrative or judicial remedies.

E. The Steering Committee shall meet within one month of the execution of this CRADA, and then regularly thereafter as appropriate.

F. The Parties shall report regularly to the Steering Committee on the progress of the various clinical trials under their supervision, and on other research and drug development efforts subject to this CRADA.

G. At the first Steering Committee meeting, and at regular intervals thereafter, the Parties shall provide to each other (1) information about the quantity of taxol available for clinical research and other research purposes pursuant to this CRADA, together with relevant stability data; and (2) anticipated timelines for drug production and supply for activities subject to this CRADA.

H. Attendance at Steering Committee meetings shall be limited to members of the Steering Committee and invited participants as mutually agreed to by the Parties.

I. The Steering Committee shall prepare, and the Parties shall approve, written summaries of each Steering Committee meeting. These summaries shall include information about Steering Committee deliberations and describe issues addressed and decisions reached. Written materials created by the Steering Committee shall be treated as described in Subparagraph J of Paragraph 1.

J. Except as required by law and subject to Paragraph 15 of this CRADA, the Parties agree that any information or documents created or exchanged pertaining to the subject matter of this CRADA, all discussions and information exchanged at meetings of the Steering Committee, and all written summaries of Steering Committee meetings shall be maintained as confidential to the Parties, and shall not be disclosed to any third-parties absent agreement by the Steering Committee.

2. FINANCIAL AND STAFFING CONTRIBUTIONS

A. Although expenses and staffing are impossible to quantify at this time, Bristol-Myers Squibb anticipates committing direct expenses of [

] dollars in furtherance of its development of taxol, and anticipates committing a minimum of [

] staff years to taxol research and development efforts.

B. NCI, in collaboration with Bristol-Myers Squibb, shall continue clinical development of taxol under NCI's extramural and intramural clinical research programs.

C. NCI will provide no funding to Bristol-Myers Squibb for collaborative research or development pursuant to this CRADA.

3. EXISTING IND

NCI has filed an investigational new drug application ("IND"), IND No. 22,850, for taxol with FDA. [

]

4. COMPLETED AND ONGOING CLINICAL TRIALS AND DATA SUBJECT TO THIS CRADA

A. NCI, directly and through its extramural research network ("extramural investigators"), has funded or conducted studies, or is funding or conducting studies, some of which

support the registration of taxol. As to such taxol studies or data currently within NCI's control, NCI shall, subject to the right of publication afforded by Paragraph 15 of this CRADA, maintain these raw data as proprietary and confidential, and make them available exclusively to Bristol-Myers Squibb for use in obtaining approval for the commercial marketing of taxol. As to government-funded taxol data currently in the control of extramural investigators, NCI shall urge extramural investigators to cooperate exclusively with Bristol-Myers Squibb in providing raw data for use in obtaining regulatory approval for the commercial marketing of taxol. However, NCI's urging is not intended to constitute a term or condition for making an award to said extramural investigators.

B. Bristol-Myers Squibb shall provide formulated taxol product for ongoing studies as provided in Paragraph 11 of this CRADA.

5. STUDIES AND DATA TO BE INITIATED PURSUANT TO THIS CRADA

A. NCI and Bristol-Myers Squibb will collaborate on the design, oversight and implementation of clinical trials required for FDA approval for the commercialization of taxol. These studies will be selected and designed to be utilized in a New Drug Application ("NDA") to obtain FDA approval for the marketing of taxol for treatment of [ ]. NCI and Bristol-Myers Squibb will supply formulated taxol product for use in these clinical trials, as recommended and prioritized by the

Steering Committee. It is anticipated, and the Parties will utilize best efforts to ensure, that an NDA [ ] will be filed within [ ] from the date of the execution of this CRADA.

B. [

]

C. Bristol-Myers Squibb shall initiate any new pre-clinical studies Bristol-Myers Squibb determines are necessary for drug registration.

D. As soon as feasible, Bristol-Myers Squibb shall provide formulated taxol product for NCI intramural studies as approved by the Steering Committee as well as the extramural trials outlined in subparagraph B of this Paragraph 5.

E. Subject to the right of publication afforded by Paragraph 15 of this CRADA, the Parties agree that all new studies and raw data developed pursuant to this Paragraph, and under their control, shall be maintained as proprietary and confidential. NCI shall make the raw data available exclusively

to Bristol-Myers Squibb for use in obtaining regulatory approval for the commercial marketing of taxol. NCI shall indicate in all future contracts with extramural investigators for taxol research and in all intramural clinical research that such data shall be so maintained, and no future extramural contract for taxol research under this Paragraph 5 shall be executed absent such investigator's concurrence regarding confidentiality. With respect to future extramural research conducted under grants from NCI, NCI shall urge extramural investigators to cooperate exclusively with Bristol-Myers Squibb in providing raw data for use in obtaining regulatory approval for the commercial marketing of taxol. However, NCI's urging is not intended to constitute a term or condition for making an award to said extramural investigators.

6. DATA COLLECTION

A. Bristol-Myers Squibb shall be responsible for collecting taxol-related pre-clinical and clinical data from investigators described in Paragraphs 4 and 5 of this CRADA.

B. In pursuing data collection efforts, Bristol-Myers Squibb shall provide funds to investigators as necessary and appropriate for all additional laboratory tests or clinical trials requested by Bristol-Myers Squibb, for data collection expenses, and for generation of case report forms.

C. It is understood that NCI will be permitted access to all data subject to this CRADA.

7. NEW DRUG APPLICATION

A. Bristol-Myers Squibb shall prepare and submit an NDA to FDA as expeditiously as is feasible, when Bristol-Myers Squibb determines that such actions are justified by clinical results.

B. NCI shall cooperate with Bristol-Myers Squibb as necessary and appropriate in all aspects of the registration process.

8. EXCHANGE OF TECHNICAL INFORMATION

A. To the extent permitted by law, and subject to appropriate confidentiality protections, NCI shall, during the term of this CRADA, provide to Bristol-Myers Squibb all technical information in its possession, or acquired in the future, regarding taxol research and development.

9. COMPLIANCE WITH HHS REGULATIONS

Bristol-Myers Squibb agrees to comply with all appropriate Department of Health and Human Services regulations relating to Human Subject Use, all applicable U.S. Department of Agriculture regulations, and all Public Health Service policies relating to the use and care of laboratory animals.

10. ADDITIONAL RESEARCH

A. Bristol-Myers Squibb shall investigate and establish, as feasible and appropriate, alternative sources of taxol. These sources shall include [

]

B. NCI shall be free to sponsor additional basic research outside the scope of this CRADA. The research outside the scope of this CRADA includes studies of basic mechanisms of taxol action, taxol production, taxol derivatives and taxol analogues, and the use of taxol for other indications not added by amendment to this CRADA pursuant to Subparagraph B of Paragraph 5. However, NCI acknowledges Bristol-Myers Squibb's need to commercialize taxol as rapidly as possible in order to make the product widely available to the oncology community and to recover the investment made in taxol research so that ongoing taxol development can be adequately financed. NCI agrees to refrain from assisting any commercial party other than Bristol-Myers Squibb for the commercialization of taxol during the term of this CRADA, and during any period thereafter in which Bristol-Myers Squibb is engaged in the commercial development and marketing of taxol, provided that this CRADA is not terminated under Subparagraphs B or C of Paragraph 17, and that public health needs are adequately served.

C. Bristol-Myers Squibb shall be free to sponsor additional clinical and pre-clinical research outside the scope of this CRADA.

11. PROCESSING AND SUPPLY OF FORMULATED TAXOL FOR CLINICAL TRIALS AND COMPASSIONATE USE

A. NCI shall transfer to Bristol-Myers Squibb *Taxus* bark collected pursuant to Contract # [

] for processing into formulated taxol product. Except as provided in Subparagraph A of Paragraph 5, and in Subparagraph B of Paragraph 11, Bristol-Myers Squibb shall acquire and process all other quantities of bulk taxol needed to fulfill the formulated taxol requirements of this CRADA as feasible and appropriate.]

B. NCI and Bristol-Myers Squibb shall supply formulated taxol, as available from existing inventories, for clinical trials as prioritized by the Steering Committee.

C. Formulated taxol product shall be supplied pursuant to this Paragraph for all clinical trials to which NCI currently has committed (<u>see</u> Exhibit A) and for future clinical trials or other research as determined by the Steering Committee.

D. [

]

12. GROUP C

A. Group C drug distribution shall be initiated when the Steering Committee recommends, and NCI and Bristol-Myers Squibb mutually agree, that such action is justified by clinical results

and feasible based on adequate drug supply. Drug for this use shall be provided [ ] to NCI by Bristol-Myers Squibb.

B. The Steering Committee will determine the quantity of drug to be made available for Group C distribution, and shall design and approve a clinical protocol to govern such distribution. In exercising these responsibilities, the Steering Committee shall consider the need of the public, the availability of alternative therapies, the availability of formulated taxol product, and the need adequately to supply ongoing clinical trials.

13. COMMERCIALIZATION OF TAXOL

A. [

]

B. [

]

C. [

]

14. INTELLECTUAL PROPERTY

A. The Parties agree that if any patentable invention is conceived or reduced to practice in the performance of collaborative research under this CRADA by employees of NCI or Bristol-Myers Squibb, such invention shall be treated in accordance with the provisions of the NIH model CRADA, and accompanying NIH policy documents, attached as Exhibit D.

B. [

15. PUBLICATION

A. As is consistent with the Parties' obligation to maintain raw data described herein confidential and proprietary, the Parties may publicly disclose the results of their research. Before either Party submits a paper or abstract for publication or otherwise intends to publicly disclose information subject to this CRADA, the other Party shall be provided thirty (30) days to review the proposed publication or disclosure to assure that confidential and proprietary data is protected. The publication or other disclosure shall be delayed for up to thirty (30) additional days upon written request by either Party as necessary to preserve U.S. or foreign or other intellectual property rights. Nothing contained in Subparagraph J of Paragraph 1 of this CRADA shall prevent the timely publication of the results of clinical trials or pre-clinical research.

B. Except as to the obligations of extramural investigators to maintain raw data as confidential and proprietary to Bristol-Myers Squibb for use in obtaining regulatory approval for the commercial marketing of taxol as described in Paragraphs 4 and 5 of this CRADA, nothing contained herein shall restrict the rights of extramural investigators to

publish the results of their research in accordance with applicable policies of NCI.

16. ABSTRACT OF THE CRADA RESEARCH PLAN FOR PUBLIC RELEASE

The following is an abstract of the CRADA Research Plan for public release:

> The National Cancer Institute and Bristol-Myers Squibb Company will collaborate in the clinical development of taxol, a novel chemically defined compound which has shown promising antitumor activity in several clinical trials. Of particular interest is the 30% objective response rate observed in Phase II trials in patients with relapsed or refractory ovarian cancer, a disease generally considered resistant to chemotherapy. The National Cancer Institute and the Bristol-Myers Squibb Company will collaborate to obtain approval of taxol as a commercial anticancer agent for this indication and to evaluate its clinical utility in other human malignancies.

17. TERMINATION

A. This CRADA may be terminated at any time by mutual consent of the Parties.

B. Either Party may terminate this CRADA if the other Party breaches a material term or condition, and if the breach is not cured within a period of sixty (60) days after written notice of breach is given to the other Party.

C. This CRADA may be terminated by Bristol-Myers Squibb if, on the basis of reasonable evidence, Bristol-Myers Squibb determines that the further development of taxol pursuant to this CRADA is not commercially feasible.

D. This CRADA may be terminated by NCI if, after providing Bristol-Myers Squibb sixty (60) days notice and a reasonable opportunity to cure, NCI determines, on the basis of reasonable evidence, that Bristol-Myers Squibb has failed to exercise best efforts in the commercialization of taxol.

E. In the event of termination of this CRADA, the disposition of the data, property, studies, and raw materials, including formulated taxol, and taxol to be formulated subject to this CRADA, shall be determined by the Steering Committee. All raw materials to be transferred to NCI pursuant to this Subparagraph shall be provided at cost by Bristol-Myers Squibb.

18. ENTIRE AGREEMENT

A. This CRADA constitutes the entire agreement in respect of the subject matter hereof between the Parties, and supersedes all previous negotiations, commitments and/or agreements, whether written or oral. It may not be changed or modified in any manner, orally or otherwise, except by an instrument in writing signed by a duly authorized officer or representative of each of the Parties.

B. For ease of scientific review and reference, a Research Plan (Exhibit B) and a Statement of Respective Contributions of the Parties (Exhibit C) are attached to this CRADA. These exhibits are abstracted from the provision of this CRADA, and the inclusion of these exhibits is not intended to

alter the rights and obligations of the Parties as set forth in the text of this CRADA.

19. NOTICES

Any notices in writing and payments to be made under this CRADA will be deemed duly given and made if sent by courier or by certified or registered mail, postage prepaid. Communications between the Parties will be addressed to the following persons, or to such other persons as the parties may designate from time to time in writing:

To NCI: (1) Director, Division of Cancer Treatment
National Cancer Institute
Building 31, Room 3A52
9000 Rockville Pike
Bethesda, Maryland 20892

and

(2) Director, Office of Technology Development
National Cancer Institute
Building 31, Room 3A52
9000 Rockville Pike
Bethesda, Maryland 20892

To Bristol-Myers Squibb: Vice President, Licensing
Bristol-Myers Squibb
P.O. Box 4000
Princeton, New Jersey 08540

20. **AUTHORITY**

By executing this CRADA, each of the undersigned represents and confirms that he is fully authorized to bind his identified company or entity to its terms.

21. **WAIVER**

The waiver by either Party of a breach of any provisions of this CRADA will not operate or be construed as a waiver of any subsequent breach.

22. **GOVERNING LAW**

The construction, validity, performance and effect of this CRADA shall be governed by Federal Law, as applied by the Federal Courts in the District of Columbia.

23. **EFFECTIVE DATE**

This CRADA shall be effective on the date last below signed.

IN WITNESS THEREOF, the Parties have caused this CRADA to be executed.

NATIONAL CANCER INSTITUTE	BRISTOL-MYERS SQUIBB COMPANY
By: Richard H. Adamson	By: John P. Haverty
Title: Acting Deputy Director	Title: Vice President, Licensing
Date: January 19, 1991	Date: January 23, 1991

MEMORANDUM OF UNDERSTANDING

BETWEEN THE DEPARTMENT OF AGRICULTURE, THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, AND THE DEPARTMENT OF THE INTERIOR REGARDING THE EFFECTIVE USE OF NATURAL PRODUCTS WITH POTENTIAL FOR THE TREATMENT OF CANCER

WHEREAS, even though there are drugs available which provide some benefit in the treatment of ovarian cancer, each year approximately 12,000 women die of this disease.

WHEREAS, taxol is a plant-derived anticancer drug discovered through research supported by the National Cancer Institute. Currently, the only source of taxol approved for use in clinical trials is the bark of the Pacific yew tree, Taxus brevifolia.

WHEREAS, in clinical trials conducted under the sponsorship of the National Cancer Institute, taxol has demonstrated significant activity against recurrent ovarian cancer with a 30-35% response rate in over 200 patients. Due to this high response rate, further research is in progress using taxol in combination with other drugs against ovarian cancer and in the treatment of other major cancers such as breast, lung and colon, and such research is an emergency priority.

WHEREAS, there is a critical shortage of taxol at the present time. More than 25 kilograms of pure taxol will be required this year to meet the immediate needs of approximately 12,000 ovarian cancer patients, to maintain and expand the clinical trials of taxol, and to begin to meet the needs of patients who are not participating in these trials. To satisfy this year's demand for taxol a minimum of 750,000 pounds of bark from the Pacific yew tree is required, and needs for the future will continue to expand.

WHEREAS, Pacific yew grows in western forests from the southern tip of Alaska, through western Washington and Oregon, to central California; in moister portions of the Blue Mountains in eastern Washington and Oregon; and in the moister western Rocky Mountains from southeastern British Columbia south to central Idaho and western Montana.

WHEREAS, the greatest concentration of existing Pacific yew is found on lands in the western United States managed by agencies within the Department of Agriculture and the Department of the Interior.

WHEREAS, the National Cancer Institute, an agency within the Department of Health and Human Services, pursuant to authority granted by the Federal Technology Transfer Act, 15 U.S.C. § 3710a, initiated an open, competitive process to select a private entity in order to facilitate the clinical and commercial development of taxol. As a result of this competitive process, the National Cancer Institute entered into a Cooperative Research and Development Agreement (CRADA) designating Bristol-Myers Squibb Company as its partner in the development of taxol.

WHEREAS, the National Cancer Institute's designee under the CRADA is required to secure adequate supplies of taxol for continued development and commercialization of the drug, including support of necessary clinical trials and distribution of taxol for compassionate use.

WHEREAS, the Secretary of Agriculture, pursuant to the National Agricultural Research, Extension, and Teaching Policy Act as amended, 7 U.S.C. §§ 3318, 3819e, may participate with private sector entities and other Federal agencies to conduct fundamental and applied research related to the development of new commercial products derived from natural plant materials for medical and other applications. Additionally, the Secretary of Agriculture under the Rangeland Renewable Resources Research Act of 1978, 16 U.S.C. §§ 1643(c), may enter into cooperative agreements with Federal and State governmental entities as well as private agencies, and may receive money and other contributions to support the protection, management, and utilization of the Nation's renewable resources.

WHEREAS, the Secretary of Health and Human Services, pursuant to 42 U.S.C. § 241 is authorized to encourage, cooperate with, and render assistance to other appropriate public authorities, scientific institutions, and scientists in the conduct of, and promote the coordination of, research, investigations, experiments, demonstrations, and studies relating to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impairments of man.

WHEREAS, the Secretary of the Interior, pursuant to Section 307 of the Federal Land Policy and Management Act of 1976, 43 U.S.C. § 1737, may conduct investigations, studies and experiments, on his own initiative or in cooperation with others, involving the management, protection, development, acquisition and conveyance of public lands and may enter into cooperative agreements for these purposes, subject to applicable laws.

WHEREAS, nothing in this Memorandum shall be construed as obligating the agencies involved to expend, contract, or otherwise commit the United States to any payment of funds in excess of appropriations authorized by law.

WHEREAS, no member of, delegate to, or resident commissioner in Congress may receive any benefit arising from this Memorandum, other than a general benefit which may be conferred upon a corporation.

NOW THEREFORE, in consideration of the above premises the Secretary of Agriculture, the Secretary of Health and Human Services, and the Secretary of the Interior agree as follows:

I. OBJECTIVES

A. Due to the urgency of the research being conducted by the National Cancer Institute, and the pressing need for taxol to carry out that research, the parties to this Memorandum shall use their best efforts, consistent with applicable laws, to assist the National Cancer Institute's designee under the CRADA in obtaining the raw material needed to produce taxol in accordance with its obligations under the CRADA.

B. In recognition of the inestimable value of Pacific yew, the parties to this Memorandum agree that it is in the national interest to promote and encourage a comprehensive research strategy designed to address the ecology, silviculture, management, and long-term viability of the Pacific yew, and to seek renewable sources of the drug.

C. The parties to this Memorandum shall use their best efforts to ensure that the raw material needed for extracting taxol is obtained in compliance with all applicable environmental laws and with minimal adverse environmental impact, and otherwise reflects environmental concern for the long-term survival of the species.

D. Due to the critical need to obtain greater quantities of taxol of suitable quality for use in research and treatment of human cancer, the parties to this Memorandum shall use their best efforts to ensure that the available raw material needed for extracting taxol is directed to those institutions which: (1) have been duly designated as agents of the National Cancer Institute's designee under the CRADA, and (2) are capable of producing taxol for human use in accordance with the Food & Drug Administration's Good Manufacturing Practices regulations. However, the parties to this Memorandum retain the right to make available, for research purposes, limited amounts of raw material to state and federal agencies, educational institutions, and other entities independent of the current ability of those entities to meet the Good Manufacturing Practices requirements.

II. Interagency Coordination

The parties to this Memorandum, recognizing the need to obtain greater quantities of taxol shall, to the extent practical, coordinate the activities of their respective agencies in the furtherance of the objectives set forth in this Memorandum. Nothing herein, however, is intended to alter, limit or expand the existing statutory authority of any of the parties to this Memorandum.

In Witness Whereof, the parties hereto have executed this Agreement as of the last date written below.

6-21-91 — Edward Madigan
(Date) — Secretary of Agriculture

June 21, 1991 — Louis W. Sullivan, M.D.
(Date) — Secretary of Health and Human Services

June 26 1991 — Manuel Lujan
(Date) — Secretary of the Interior

COOPERATIVE AGREEMENT
BETWEEN THE
UNITED STATES DEPARTMENT OF AGRICULTURE
FOREST SERVICE
AND
BRISTOL-MYERS SQUIBB COMPANY

THIS COOPERATIVE AGREEMENT is made and entered into by and between Bristol-Myers Squibb Company (hereinafter referred to as the Cooperator), and the Forest Service, U.S. Department of Agriculture (hereinafter referred to as the Forest Service).

WHEREAS, the Federal Technology Transfer Act, 15 U.S.C. 3710a, authorizes the federal government to enter into Cooperative Research and Development Agreements (CRADAs) with private entities for the development of new products and technologies;

WHEREAS, the Cooperator has entered into a CRADA with the National Cancer Institute (NCI), a component of the Department of Health and Human Services, in accordance with which Cooperator has been designated, through a competitive process, as NCI's sole commercial partner for purposes of the clinical and commercial development of taxol, an investigational new drug that has shown promising antitumor activity;

WHEREAS, the provisions of the NCI CRADA require the Cooperator to secure adequate supplies of taxol for continued development and commercialization of taxol, including support of necessary clinical trials and distribution of taxol through compassionate use and Group C mechanisms; to investigate the extraction, production and use of taxol; to prepare and submit a new drug application to the Food & Drug Administration to obtain approval to market the drug; and to investigate and establish alternative sources of taxol;

WHEREAS, the expeditious clinical and commercial development of taxol has been designated as a matter of highest priority by the NCI, which has stated that there is an urgent need to obtain greater quantities of taxol;

WHEREAS, at the present time, taxol is derived primarily from the bark of the PACIFIC YEW (Taxus brevifolia), resulting in an immediate and pressing need for increased supplies of PACIFIC YEW for taxol production to meet the NCI's goals for taxol development;

WHEREAS, the Forest Service is responsible for the management and development of natural resources from the National Forests, including those located in the northwestern United States which contain a substantial portion of the available supply of PACIFIC YEW;

WHEREAS, the total supply of PACIFIC YEW is limited, and the supply available from the National Forests is essential to support continuing taxol research and development;

WHEREAS, the Forest Service and the Cooperator recognize the need to:

a. Conduct inventories to determine the occurrence, quantity, and quality of PACIFIC YEW on federal lands, including the National Forests;

b. Conduct research on the ecology, silviculture, and management of PACIFIC YEW and associated species; and

c. Develop and implement management practices and guidelines that take into consideration environmental concerns relating to sound harvesting, regeneration, and sustainability of PACIFIC YEW.

WHEREAS, the Forest Service has limited financial resources available to carry out the necessary conservation, environmental, administrative and research activities commensurate with an increased level of utilization of the PACIFIC YEW for taxol research and development;

WHEREAS, the National Forest Management Act, 16 U.S.C. 472a and implementing regulations set forth at 36 CFR 223.2(c) (entitled "Disposal of Timber for Administrative Use") authorize the Forest Service to dispose of trees, portions of trees, or other forest products needed for research; and

WHEREAS, the Forest Service, pursuant to the Rangeland Renewable Resources Research Act of 1978, 16 U.S.C. 1643(c); the National Agricultural Research, Extension, and Teaching Policy Act of 1977, 7 U.S.C. 3318; Pub. L. No. 101-512, 31 U.S.C. 6305; and 7 CFR 2.42 (c), may enter into cooperative agreements with private parties, and may receive money and other contributions from cooperators under such conditions as the Chief of the Forest Service may prescribe;

WHEREAS, the Cooperator has entered into a similar cooperative agreement with the United States Department of the Interior, Bureau of Land Management;

NOW THEREFORE, in consideration of the above premises, the parties hereto agree as follows:

A. Definitions:

As used in this agreement, ANNUAL PACIFIC YEW PROGRAM PLANS, and other implementing documents, the following terms have these definitions:

1. <u>ANNUAL PACIFIC YEW PROGRAM PLANS</u> -- Written annual plans, prepared and mutually agreed upon by the Cooperator and the Forest Service, to implement this agreement through specified PROGRAM ELEMENTS.

2. <u>AUTHORIZED OFFICER</u> -- A government employee authorized to execute and administer the transfer of Pacific yew to Cooperator through permits, timber sales, or other contracts.

3. <u>PACIFIC YEW</u> -- All portions of <u>Taxus</u> <u>brevifolia</u>, including but not limited to bark, twigs, needles and other foliage.

4. <u>PROGRAM ELEMENTS</u> -- Detailed descriptions of research projects, environmental documents, PACIFIC YEW inventories, guidelines for the management and preservation of the PACIFIC YEW, harvesting goals and methods, funding requirements, and other related tasks and activities necessary to implement this agreement as mutually agreed upon in ANNUAL PACIFIC YEW PROGRAM PLANS.

B. **The Forest Service shall:**

1. After consultation with the Cooperator and the Bureau of Land Management, develop and implement a comprehensive program for conducting research on the ecology, silviculture, and management of PACIFIC YEW and associated species, for managing the utilization of PACIFIC YEW obtained from National Forest lands to support taxol research and development purposes in a manner which reflects environmental concern for the long-term survival of the species, and for assuring that all PACIFIC YEW harvested in accordance with this agreement are transferred to the Cooperator, subject to applicable laws, regulations, and forest plans for the affected area, and subject to approval by the responsible AUTHORIZED OFFICER. This program may include, but is not limited to, preparation of an inventory of PACIFIC YEW located on federal land, development of guidelines for the management and utilization of PACIFIC YEW in an environmentally sound manner, preparation of necessary environmental documents, execution of research on the ecology, silviculture, and management of the PACIFIC YEW and associated species, and other related activities, as agreed upon in ANNUAL PACIFIC YEW PROGRAM PLANS.

2. Designate contact persons and representatives to meet annually with appropriate representatives of the Cooperator and the Bureau of Land Management to discuss and agree upon coordinated ANNUAL PACIFIC YEW PROGRAM PLANS containing PROGRAM ELEMENTS, including detailed descriptions of research projects and funding levels, necessary to implement this agreement. On a quarterly basis, these representatives will review implementation of this agreement and ANNUAL PACIFIC YEW PROGRAM PLANS, discuss and resolve problems arising thereunder, and generally coordinate Yew Program activities.

3. Use its best efforts to develop ANNUAL PACIFIC YEW PROGRAM PLANS, PROGRAM ELEMENTS, and related cost estimates in accordance with general funding levels set forth in Schedule A. Although Cooperator agrees that it will not hold the Forest Service liable for damages for inaccurate cost and PACIFIC YEW volume estimates, the Cooperator reserves the right to refuse to fund individual PROGRAM ELEMENTS that exceed funding levels agreed upon in the ANNUAL PACIFIC YEW PROGRAM PLANS.

4. Furnish all personnel and administrative services needed to conduct research on the ecology, silviculture, and management of the PACIFIC YEW

and associated species, to administer timber sale contracts and permits for harvesting of PACIFIC YEW, and to document, approve and implement this agreement and ANNUAL PACIFIC YEW PROGRAM PLANS agreed to by the Cooperator.

5. Provide prompt written notice to Cooperator of each permit, timber sale, or other contract under which PACIFIC YEW located on National Forest System lands will be available for transfer to Cooperator in accordance with this agreement.

6. Provide prompt written notice to Cooperator of all instances in which Cooperator or its agents, contractors, or subcontractors are failing to comply with the terms of this agreement, with the terms of applicable ANNUAL PACIFIC YEW PROGRAM PLANS and implementing permits, timber sales, or other contracts, and with applicable environmental protection standards as enunciated or required by the Forest Service.

7. Keep such records as are required for Forest Service approval and administration of this agreement, ANNUAL PACIFIC YEW PROGRAM PLANS, and all projects initiated in accordance with this agreement, and provide Cooperator with quarterly accountings of funds expended in accordance with this agreement and implementing documents.

8. Comply with provisions of Executive Order 12600, 52 Fed. Reg. 23,781 (1987), with respect to the confidential treatment of commercial and financial information contained in this agreement or obtained by the Forest Service in connection with this agreement.

C. The Cooperator shall:

1. Assure that all PACIFIC YEW obtained in accordance with this agreement will be utilized to the fullest extent practicable to produce taxol in accordance with the Cooperator's obligations under its CRADA with NCI. The disposition of any PACIFIC YEW which Cooperator cannot otherwise practicably utilize to produce taxol will be mutually agreed upon by the Cooperator and the Forest Service in ANNUAL PACIFIC YEW PROGRAM PLANS.

2. Accept or reject each transfer of PACIFIC YEW offered by the Forest Service within 30 days of receiving written notice of the availability of the applicable permit, timber sale, or other contract. Any offer of PACIFIC YEW which is rejected by Cooperator may subsequently be offered by the Forest Service to parties outside of this agreement.

3. Perform all administrative tasks required for the employment of agents, contractors, or subcontractors to carry out the terms of any permits, timber sales, or other contracts used to convey PACIFIC YEW to Cooperator in accordance with this agreement.

4. Furnish to the Forest Service the names, addresses and business locations of firms or individuals authorized to act as Cooperator's agents,

contractors, or subcontractors for purposes of procuring and harvesting PACIFIC YEW in accordance with this agreement.

5. Use its best efforts to assure that the Cooperator and its agents, contractors and subcontractors comply with all terms and conditions of permits, timber sales, or other contracts entered into for the purpose of conveying PACIFIC YEW to the Cooperator in accordance with this agreement.

6. Use its best efforts to assure that, with respect to all activities undertaken in accordance with this agreement, the Cooperator and its agents comply with all applicable environmental protection standards as enunciated or required by the Forest Service.

7. Designate contact persons and representatives to meet annually with appropriate Forest Service and Bureau of Land Management representatives to discuss and agree upon coordinated ANNUAL PACIFIC YEW PROGRAM PLANS containing PROGRAM ELEMENTS, including detailed descriptions of research projects and funding levels, necessary to implement this agreement. On a quarterly basis, these representatives shall review implementation of this agreement and ANNUAL PACIFIC YEW PROGRAM PLANS, discuss and resolve problems arising thereunder, and generally coordinate Yew Program activities.

8. Provide funds needed to implement ANNUAL PACIFIC YEW PROGRAM PLANS as agreed upon by the Cooperator.

9. Request no records or reports from the Forest Service, except those that may be needed for administration of permits, timber sale contracts or other related contracts used to implement this agreement.

10. Hold the Forest Service harmless from any and all claims, liability or damages incurred by the Cooperator, or the Cooperator's agents, contractors, or subcontractors in connection with activities authorized by this agreement.

11. Provide prompt notice to the Forest Service in the event that the Cooperator's CRADA with NCI is terminated or materially modified during the term of this agreement.

D. It is mutually agreed that:

1. Transfer of PACIFIC YEW will be accomplished in accordance with the terms of this agreement, ANNUAL PACIFIC YEW PROGRAM PLANS, and all implementing permits, timber sales, or other contracts negotiated between the Forest Service and the Cooperator.

2. Transfer of PACIFIC YEW to persons or entities other than Cooperator will be limited, in each permit, timber sale, or other contract, to *de minimis* amounts to be specified in ANNUAL PACIFIC YEW PROGRAM PLANS developed pursuant to this agreement;

3. The Forest Service retains the right to make PACIFIC YEW available to state and federal agencies, educational institutions, and other entities in de minimis amounts to be specified in ANNUAL PACIFIC YEW PROGRAM PLANS developed pursuant to this agreement.

4. Research conducted under this agreement may include study of the ecology, silviculture, and management of the PACIFIC YEW and associated species, preparation of an inventory of the species located on federal land, analysis of environmentally sound harvesting methods, and related activities, as approved by Cooperator.

5. Research findings on the ecology, silviculture, and management of PACIFIC YEW and associated species will be shared with Cooperator, but will remain the property of the Federal Government. These findings may be published at the discretion of the Forest Service.

6. The parties will coordinate press releases and other public statements concerning this agreement, ANNUAL PACIFIC YEW PROGRAM PLANS and implementing documents.

7. ANNUAL PACIFIC YEW PROGRAM PLANS and implementing permits, timber sales, and other contracts shall be treated as subordinate to, and shall not take precedence over, the rights and obligations established by this agreement.

8. To the extent practicable, this agreement shall be implemented and construed in a manner consistent with a similar cooperative agreement between the Cooperator and the Department of Interior, Bureau of Land Management.

9. Nothing in this agreement shall be construed as obligating the Forest Service to expend, contract, or otherwise commit the United States to future payment of funds in excess of appropriations authorized by law.

10. Either party may terminate this agreement by providing written notice at least 90 days prior to the date of intended termination.

11. Notwithstanding the termination provision in paragraph D. 10 of this agreement, the Forest Service may at any time suspend or terminate harvesting of PACIFIC YEW pursuant to this agreement, in whole or in part, to comply with any court order, administrative decision, statute, or regulation, or to prevent serious environmental harm as determined by the Forest Service.

12. In the event this agreement is suspended or terminated, such suspension or termination shall be without compensation to the non-terminating party, except that any of Cooperator's funds on deposit with the Forest Service will remain available to cover expenses rising out of, or incident to, work initiated prior to the date of such suspension or termination. After such work is completed, any of Cooperator's remaining

funds deposited with the Forest Service shall be returned to the Cooperator within 30 days.

13. Notice required by this agreement shall be provided in writing to the following persons:

For the Forest Service: ____________________

For the Cooperator: ____________________

14. This agreement may not be orally modified. Amendments to this agreement are valid only if they are in writing and signed by both the Cooperator and the Forest Service.

15. The duration of this agreement shall be five years from the date of execution, subject to the renewal of this agreement for additional periods of one year as mutually agreed upon by the parties.

16. Unless terminated in writing, this agreement will remain in force until the expiration date.

17. Disputes arising under this agreement which cannot be resolved by the representatives identified in paragraphs B. 2 and C. 7 shall be referred to the two signatories of this agreement for resolution.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the last date written below.

6-14-91
(Date)

Edward Madigan
EDWARD MADIGAN
Secretary of Agriculture

6 19-91
(Date)

Z. Horovitz
DR. ZOLA HOROVITZ
Senior Vice President
Bristol-Myers Squibb

COOPERATIVE AGREEMENT
BETWEEN THE
UNITED STATES DEPARTMENT OF THE INTERIOR
BUREAU OF LAND MANAGEMENT
AND
BRISTOL-MYERS SQUIBB COMPANY

THIS COOPERATIVE AGREEMENT is made and entered into by and between Bristol-Myers Squibb Company (hereinafter referred to as the Cooperator), the Bureau of Land Management and the U.S. Department of the Interior (hereinafter referred to as the Bureau of Land Management).

WHEREAS, the Federal Technology Transfer Act, 15 U.S.C. § 3710a, authorizes the federal government to enter into Cooperative Research and Development Agreements (CRADAs) with private entities for the development of new products and technologies;

WHEREAS, the Cooperator has entered into a CRADA with the National Cancer Institute (NCI), a component of the Department of Health and Human Services, in accordance with which Cooperator has been designated, through a competitive process, as NCI's sole commercial partner for purposes of the clinical and commercial development of taxol, an investigational new drug that has shown promising antitumor activity;

WHEREAS, the provisions of the NCI CRADA require the Cooperator to secure adequate supplies of taxol for continued development and commercialization of taxol, including support of necessary clinical trials and supply of taxol through compassionate use distribution channels; to investigate the extraction, production and use of taxol; to prepare and submit a new drug application to the Food & Drug Administration to obtain approval to market the drug; and to investigate and establish alternative sources of taxol;

WHEREAS, the expeditious clinical and commercial development of taxol has been designated as a matter of highest priority by the NCI, which has stated that there is an urgent need to obtain greater quantities of taxol;

WHEREAS, at the present time, taxol is derived primarily from the bark of the PACIFIC YEW (<u>Taxus</u> <u>brevifolia</u>), resulting in an immediate and pressing need for increased supplies of PACIFIC YEW for taxol production to meet the NCI's goals for taxol development;

WHEREAS, the Bureau of Land Management is responsible for the management and development of natural resources on public lands, including forests located in the northwestern United

States which contain a substantial portion of the available supply of PACIFIC YEW;

WHEREAS, the total supply of PACIFIC YEW is limited, and the supply available from Bureau of Land Management administered public lands is essential to support continuing taxol research and development;

WHEREAS, the Bureau of Land Management and the Cooperator recognize the need to:

- **a.** Conduct inventories to determine the occurrence, quantity, and quality of PACIFIC YEW on public lands;
- **b.** Conduct research on the ecology, silviculture, and management of PACIFIC YEW and associated species; and
- **c.** Develop and implement management practices and guidelines that take into consideration environmental concerns relating to sound harvesting, regeneration, and sustainability of PACIFIC YEW.

WHEREAS, the Bureau of Land Management has limited financial resources available to carry out the necessary conservation, environmental, administrative and research activities commensurate with an increased level of utilization of the PACIFIC YEW for taxol research and development;

WHEREAS, Section 307 of the Federal Land Policy and Management Act of 1976, 43 U.S.C. § 1737, provides that the Secretary of the Interior may conduct investigations, studies and experiments, on his own initiative or in cooperation with others, involving the management, protection, development, acquisition and conveyance of public lands and may enter into cooperative agreements for these purposes, subject to applicable laws;

WHEREAS, the Cooperator has entered into a similar cooperative agreement with the Forest Service, United States Department of Agriculture;

NOW THEREFORE, in consideration of the above premises, the parties hereto agree as follows:

A. **Definitions:**

As used in this agreement, ANNUAL PACIFIC YEW PROGRAM PLANS, and other implementing documents, the following terms have these definitions:

1. ANNUAL PACIFIC YEW PROGRAM PLANS -- Written annual plans, prepared and mutually agreed upon by the Cooperator and the Bureau of Land Management, to implement this agreement through specified PROGRAM ELEMENTS.

2. AUTHORIZED OFFICER -- A government employee authorized to execute and administer the transfer of Pacific yew to Cooperator through permits, timber sales, or other contracts.

3. PACIFIC YEW -- All portions of *Taxus brevifolia*, including but not limited to bark, twigs, needles and other foliage.

4. PROGRAM ELEMENTS -- Detailed descriptions of research projects, environmental documents, PACIFIC YEW inventories, guidelines for the management and preservation of the PACIFIC YEW, harvesting goals and methods, funding requirements, and other related tasks and activities necessary to implement this agreement as mutually agreed upon in ANNUAL PACIFIC YEW PROGRAM PLANS.

B. **The Bureau of Land Management shall:**

1. After consultation with the Cooperator and the Forest Service, develop and implement a comprehensive program for conducting research on the ecology, silviculture, and management of PACIFIC YEW and associated species, for managing the utilization of PACIFIC YEW obtained from public lands to support taxol research and development purposes in a manner which reflects environmental concern for the long-term survival of the species, and for assuring that PACIFIC YEW harvested in accordance with this agreement are transferred to the Cooperator, subject to applicable laws, regulations, and forest plans for the affected area, and subject to approval by the responsible AUTHORIZED OFFICER. This program may include, but is not limited to, preparation of an inventory of PACIFIC YEW located on public land, development of guidelines for the management and utilization of PACIFIC YEW in an environmentally sound manner, preparation of necessary environmental documents, execution of appropriate transfer documents, execution of research on the ecology, silviculture, and management of the PACIFIC YEW

and associated species, and other related activities, as agreed upon in ANNUAL PACIFIC YEW PROGRAM PLANS.

2. Designate contact persons and representatives to meet annually with appropriate representatives of the Cooperator and the Forest Service to discuss and agree upon coordinated ANNUAL PACIFIC YEW PROGRAM PLANS containing PROGRAM ELEMENTS, including detailed descriptions of research projects and funding levels, necessary to implement this agreement. On a quarterly basis, these representatives will review implementation of this agreement and ANNUAL PACIFIC YEW PROGRAM PLANS, discuss and resolve problems arising thereunder, and generally coordinate Yew Program activities.

3. Use its best efforts to develop ANNUAL PACIFIC YEW PROGRAM PLANS, PROGRAM ELEMENTS, and related cost estimates in accordance with general funding levels set forth in Schedule A. Although Cooperator agrees that it will not hold the Bureau of Land Management liable for damages for inaccurate cost and PACIFIC YEW volume estimates, the Cooperator reserves the right to refuse to fund individual PROGRAM ELEMENTS that exceed funding levels agreed upon in the ANNUAL PACIFIC YEW PROGRAM PLANS.

4. Furnish all personnel and administrative services needed to conduct research on the ecology, silviculture, and management of the PACIFIC YEW and associated species, to administer timber sale contracts and permits for harvesting of PACIFIC YEW, and to document, approve and implement this agreement and ANNUAL PACIFIC YEW PROGRAM PLANS agreed to by the Cooperator.

5. Provide prompt written notice to Cooperator of each permit, timber sale, or other contract under which PACIFIC YEW located on public lands will be available for transfer to Cooperator in accordance with this agreement.

6. Provide prompt written notice to Cooperator of all instances in which Cooperator or its agents, contractors, or subcontractors are failing to comply with the terms of this agreement, with the terms of applicable ANNUAL PACIFIC YEW PROGRAM PLANS and implementing permits, timber sale contracts, or other contracts, and with applicable environmental protection standards as enunciated or required by the Bureau of Land Management.

7. Keep such records as are required for Bureau of Land Management approval and administration of this agreement, ANNUAL PACIFIC YEW PROGRAM PLANS, and all projects initiated in accordance with this agreement, and provide Cooperator

with quarterly accountings of funds expended in accordance with this agreement and implementing documents.

8. Comply with provisions of Executive Order 12600, 52 Fed. Reg. 23,781 (1987), with respect to the confidential treatment of commercial and financial information contained in this agreement or obtained by the Bureau of Land Management in connection with this agreement.

C. **The Cooperator shall:**

1. Assure that all PACIFIC YEW obtained in accordance with this agreement will be utilized to the fullest extent practicable to produce taxol in accordance with the Cooperator's obligations under its CRADA with NCI. The disposition of any PACIFIC YEW which Cooperator cannot otherwise practicably utilize to produce taxol will be mutually agreed upon by the Cooperator and the Bureau of Land Management in ANNUAL PACIFIC YEW PROGRAM PLANS.

2. Accept or reject each transfer of PACIFIC YEW offered by the Bureau of Land Management within 30 days of receiving written notice of the availability of the applicable permit, timber sale contract, or other contract. Any offer of PACIFIC YEW which is rejected by Cooperator may subsequently be offered by the Bureau of Land Management to parties outside of this agreement.

3. Perform all administrative tasks required for the employment of agents, contractors, or subcontractors to carry out the terms of any permits, timber sales, or other contracts used to convey PACIFIC YEW to Cooperator in accordance with this agreement.

4. Furnish to the Bureau of Land Management the names, addresses and business locations of firms or individuals authorized to act as Cooperator's agents, contractors, or subcontractors for purposes of procuring and harvesting PACIFIC YEW in accordance with this agreement.

5. Use its best efforts to assure that the Cooperator and its agents, contractors and subcontractors comply with all terms and conditions of permits, timber sale contracts, or other contracts entered into for the purpose of conveying PACIFIC YEW to the Cooperator in accordance with this agreement.

6. Use its best efforts to assure that, with respect to all activities undertaken in accordance with this agreement, the Cooperator and its agents comply with all applicable

environmental protection standards as enunciated or required by the Bureau of Land Management.

7. Designate contact persons and representatives to meet annually with appropriate Forest Service and Bureau of Land Management representatives to discuss and agree upon coordinated ANNUAL PACIFIC YEW PROGRAM PLANS containing PROGRAM ELEMENTS, including detailed descriptions of research projects and funding levels, necessary to implement this agreement. On a quarterly basis, these representatives shall review implementation of this agreement and ANNUAL PACIFIC YEW PROGRAM PLANS, discuss and resolve problems arising thereunder, and generally coordinate Yew Program activities.

8. Provide funds needed to implement ANNUAL PACIFIC YEW PROGRAM PLANS as agreed upon by the Cooperator.

9. Request no records or reports from the Bureau of Land Management, except those that may be needed for administration of permits, timber sale contracts or other related contracts used to implement this agreement.

10. Hold the Bureau of Land Management harmless from any and all claims, liability or damages incurred by the Cooperator, or the Cooperator's agents, contractors, or subcontractors in connection with activities authorized by this agreement.

11. Provide prompt notice to the Bureau of Land Management in the event that the Cooperator's CRADA with NCI is terminated or materially modified during the term of this agreement.

12. Not advertise this agreement or any contract or transaction executed hereunder in such a manner as to state or imply that the Bureau of Land Management endorses a product, project, or commercial line of endeavor.

D. It is mutually agreed that:

1. Transfer of PACIFIC YEW to the Cooperator will be accomplished in accordance with the terms of this agreement, ANNUAL PACIFIC YEW PROGRAM PLANS, and all implementing permits, timber sale contracts, or other contracts negotiated between the Bureau of Land Management and the Cooperator.

2. Transfer of PACIFIC YEW to persons or entities other than Cooperator will be limited, in each permit, timber

sale, or other contract, to *de minimis* amounts to be specified in ANNUAL PACIFIC YEW PROGRAM PLANS developed pursuant to this agreement;

3. The Bureau of Land Management retains the right to make PACIFIC YEW available to state and federal agencies, educational institutions, and other entities in *de minimis* amounts to be specified in ANNUAL PACIFIC YEW PROGRAM PLANS developed pursuant to this agreement.

4. Research conducted under this agreement may include study of the ecology, silviculture, and management of the PACIFIC YEW and associated species, preparation of an inventory of the species located on public lands, analysis of environmentally sound harvesting methods, and related activities, as agreed upon in ANNUAL PACIFIC YEW PROGRAM PLANS.

5. Research findings on the ecology, silviculture, and management of the PACIFIC YEW and associated species, the inventory of the species located on public lands, analysis of environmentally sound harvesting methods, and related activities will be shared with the Cooperator, but will remain the property of the Federal Government. These findings may be published at the discretion of the Bureau of Land Management.

6. The Cooperator will submit to the Bureau of Land Management for approval prior to distribution all proposed press releases referring to this agreement, the Bureau of Land Management or the Department of the Interior, or the title of any employee thereof. The Bureau of Land Management will coordinate press releases and other public statements concerning this agreement, ANNUAL PACIFIC YEW PROGRAM PLANS, and implementing documents with the Cooperator.

7. In the event of a conflict between this agreement and any element of the ANNUAL PACIFIC YEW PROGRAM PLANS, implementing permits, contracts for the sale of yew or other contracts contemplated and authorized by this agreement, this agreement shall control.

8. To the extent practicable, this agreement shall be implemented and construed in a manner consistent with a similar cooperative agreement between the Cooperator and the Forest Service, Department of Agriculture.

9. Nothing in this agreement shall be construed as obligating the Bureau of Land Management to expend, contract, or otherwise commit the United States to future

payment of funds in excess of appropriations authorized by law.

10. Either party may terminate this agreement by providing written notice at least 90 days prior to the date of intended termination.

11. Notwithstanding the termination provision in paragraph D. 10 of this agreement, the Bureau of Land Management may at any time suspend or terminate harvesting of PACIFIC YEW pursuant to this agreement, in whole or in part, to comply with any court order, administrative decision, statute, or regulation, or to prevent serious environmental harm as determined by the Bureau of Land Management.

12. In the event this agreement is suspended or terminated, such suspension or termination shall be without compensation to the non-terminating party, except that any of Cooperator's funds on deposit with the Bureau of Land Management will remain available to cover expenses rising out of, or incident to, work initiated prior to the date of such suspension or termination. After such work is completed, any of Cooperator's remaining funds deposited with the Bureau of Land Management shall be returned to the Cooperator within 30 days.

13. Notice required by this agreement shall be provided in writing to the following persons:

Chief of Forestry
Bureau of Land Management
U.S. Department of the Interior
1849 C Street, N.W.
Washington, D.C. 20240

For the Cooperator:

M. Dianne DeFuria
Director, Licensing
Bristol-Myers Squibb
Route 206 & Province Line Road
Princeton, New Jersey 08540

14. This agreement may not be orally modified. Amendments to this agreement are valid only if they are in writing and signed by both the Cooperator and the Bureau of Land Management.

15. The duration of this agreement shall be five years from the date of execution, subject to the renewal of this agreement for additional periods of one year as mutually agreed upon by the parties.

16. Unless terminated in writing, this agreement will remain in force until the expiration date.

17. Disputes arising under this agreement which cannot be resolved by the representatives identified in paragraphs B. 2 and C. 7 shall be referred to the two signatories of this agreement for resolution.

18. No member of, delegate to, or resident commissioner in Congress shall be admitted to any share or part of this agreement, or to any benefit that may arise therefrom, but this provision shall not be construed to extend to this agreement if made with a corporation for its general benefit.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the last date written below.

6/4/91
(Date)

BRISTOL-MYERS SQUIBB

6/19/91
(Date)

BLM

ANNUAL PACIFIC YEW PROGRAM PLAN
Forest Service
Fiscal Year 1992

I. Introduction

The goal of this Forest Service FY 1992 Annual Pacific Yew Program Plan (1992 Plan) is to implement a Cooperative Agreement between Bristol-Myers Squibb Company (B-MS) and the Department of Agriculture/Forest Service (Forest Service). B-MS has entered into a similar Cooperative Agreement with the Department of Interior/Bureau of Land Management (BLM).

These Cooperative Agreements serve two principal purposes. First, they are part of a comprehensive federal strategy outlined in a Memorandum of Understanding (MOU) between the Department of Agriculture, the Department of Health and Human Services, and the Department of the Interior. This MOU expresses the commitment of these agencies to using their best efforts to ensure that adequate quantities of Pacific yew are available from the National Forests and other public lands to support the expeditious research and development of taxol. Taxol is a promising anticancer agent that is being developed pursuant to a Cooperative Research and Development Agreement (CRADA) between B-MS and the National Cancer Institute (NCI).

Second, the Cooperative Agreements reflect a commitment to maintaining the long-term viability of the Pacific yew in forest ecosystems throughout its current range, as they create a comprehensive research program to study the ecology, silviculture and management of the species.

This 1992 Plan will provide details about the administration of the Cooperative Agreement between B-MS and the Forest Service, the research to be conducted pursuant to this Plan, the bark transfer process, programmatic NEPA compliance, the parties' harvesting goals, and funding requirements for fiscal year 1992, which ends September 30, 1992.

II. Definitions

A. <u>PACIFIC YEW</u> -- The Cooperative Agreement defines Pacific yew to include all portions of <u>Taxus brevifolia</u> including, but not limited to, bark, twigs, needles and other foliage. It is agreed that Pacific yew is broadly

defined to maintain maximum authority on the part of Forest Service officers in designating Pacific yew for transfer. Forest Service officers are under no mandate to transfer the entire Pacific yew tree to B-MS, although the Cooperative Agreement and implementing Annual Pacific Yew Program Plans would allow them to do so.

B. <u>DESIGNATED AGENT</u> -- An agent hired by B-MS to perform the functions necessary to harvest or collect Pacific yew offered for transfer to B-MS by the Forest Service. At this time, Hauser Chemical Research, Inc., and its subsidiary Hauser Northwest, Inc., (Hauser) will act as a Designated Agent of B-MS. B-MS may change its Designated Agent(s) or authorize other entities to act as Designated Agents upon written notification to the Forest Service.

C. <u>DESIGNATED AGENT'S REPRESENTATIVE</u> -- A representative named in writing by a Designated Agent who has delegated authority to receive notices and to take action regarding the administration of assigned Pacific yew transfer permits, timber sales, or other contracts. Other authorities may be delegated in writing by a Designated Agent.

D. <u>FIELD SUPERVISOR</u> -- A person designated in writing, and responsible to, either a Designated Agent or a Designated Agent's Representative having delegated responsibility for the supervision of Pacific yew harvest activities undertaken by Harvesters.

E. <u>HARVESTERS</u> -- Peelers, loggers, gleaners, transporters, and other persons under the control and on-the-ground supervision of a Designated Agent, a Designated Agent's Representative, or a Field Supervisor. Harvesters are authorized to collect or harvest Pacific yew for a Designated Agent.

F. <u>AUTHORIZED OFFICER</u> -- A Forest Service employee authorized to execute and administer the transfer of Pacific yew to B-MS through permits, timber sales, or other contracts. "Authorized Officer" includes that person's designated representative when acting within the scope of their authority, or their duly appointed successor.

III. Administration

A. <u>In General</u>

1. To the extent practicable, the Forest Service, the BLM, and B-MS will coordinate the activities, programs, and projects undertaken pursuant to the

Cooperative Agreements and implementing Annual Pacific Yew Program Plans.

2. All activities undertaken pursuant to the Cooperative Agreements and Annual Pacific Yew Program Plans will be consistent with the MOU between the Department of Agriculture, the Department of Health and Human Services, and the Department of the Interior.

B. Meetings

1. Appropriate representatives from the Forest Service, the BLM, and B-MS will meet on an annual basis to discuss and agree upon Annual Pacific Yew Program Plans. Throughout the term of the Cooperative Agreements, annual meetings will be held in August or September of each year on a mutually agreeable date.

2. Quarterly meetings will be held during the first month of each quarter of the fiscal year on a mutually agreeable date. At these quarterly meetings, or as otherwise appropriate, the representatives of the aforementioned parties will review implementation of the Cooperative Agreements and Annual Pacific Yew Program Plans, discuss and resolve problems arising thereunder, and generally coordinate Yew Program activities. The quarterly meetings will begin during the second quarter of fiscal year 1992. These meetings may be conducted via telephone conference call if agreed upon by the parties.

3. Thirty days prior to the quarterly and annual meeting dates, the Forest Service Region 6 Yew Coordinator will notify the representatives listed below of pertinent details, including the date, time, and place of the meetings. The 30-day notice requirement may be waived with respect to a particular meeting by mutual consent of the parties.

4. In FY 1992, the Forest Service appoints the following representatives or their designated substitutes to meet at the quarterly and annual meetings:

Washington Office Coordinator
Richard Miller

Region 1 Coordinator
Merrill Davis

Region 5 Coordinator
Mike Srago

Region 6 Coordinator
Fred Page

Pacific Northwest Station Coordinator
Pete Owston

National Forest at-large Representative
Jack Schlotter, Rogue River N.F.

5. For FY 1992, B-MS appoints the following representative to meet at the quarterly and annual meetings: M. Dianne DeFuria, Senior Director, Business Development & Planning, Bristol-Myers Squibb Co., Pharmaceutical Group, Post Office Box 4000, Princeton, N.J. 08540. Ms. DeFuria may, from time to time, designate other persons to accompany her to meetings, and/or to act as an official representative of B-MS.

6. For FY 1992, BLM appoints the following representative to meet at the quarterly and annual meetings: Kent Tresidder, Oregon State Office of BLM; P.O. Box 2965; Portland, Oregon 97208.

7. Additional meetings may be held as needed, particularly during the harvesting season, to implement the Cooperative Agreements and the Annual Pacific Yew Program Plans. If the topics to be discussed at these additional meetings are specific to either the Forest Service or the BLM, then the other agency may choose not to participate in the meetings.

C. <u>Records</u>

1. The Forest Service will keep such records as are required for the agency's approval and administration of the Cooperative Agreement, Annual Pacific Yew Program Plans, and all projects initiated thereunder.

2. Any request for copies of documents other than those approved for release by Cooperator, including the Cooperative Agreement, the Annual Pacific Yew Program Plans, or other related documents must be in writing and comply with the Freedom of Information Act, 5 U.S.C. § 552 (FOIA).

3. B-MS shall submit to the Forest Service copies of redacted versions of the Cooperative Agreement, Annual Pacific Yew Program Plans, and other related documents that it considers appropriate for release to the public. These redacted versions will omit information that B-MS considers to be confidential commercial or financial information. If Forest Service personnel decide to release documents other than these redacted versions, then the agency must notify B-MS of its intent to release the designated information prior to its actual distribution. See Executive Order 12,600, 52 Fed. Reg. 23,781 (June 23, 1987). (See Attachment 1.)

IV. Program Elements

A. Pacific Yew Inventory

1. In FY 1991, the Forest Service initiated comprehensive inventories of existing Pacific yew located in portions of seven National Forests in the Cascade Mountain Range in Washington and Oregon, and one National Forest within the South Fork Clearwater River drainage in Idaho.

2. Pursuant to a similar Cooperative Agreement between B-MS and BLM, the BLM will conduct a comprehensive inventory of existing Pacific yew located on portions of public lands under its administration in Western Oregon. To the extent practicable, the Forest Service and the BLM will coordinate their efforts, data, and analyses regarding these Pacific yew inventories.

3. The initial step in conducting the National Forests Pacific Yew Inventories was the identification of conditions where Pacific yew probably will occur. The Forest Service utilized existing ecological information to develop a vegetative data base which was used to develop criteria for predicting probable locations of Pacific yew. Models using the identified criteria were developed by a team consisting of an ecologist from the National Forests and an ecologist from Forest Service Research. Using procedures previously developed for vegetative mapping, maps delineating probable and highly probable locations of Pacific yew were produced for each of the seven National Forests in the Cascade Mountains and the National Forest within the South Fork Clearwater drainage in Idaho. The mapping procedures and techniques using

satellite imagery have been reviewed by a peer group. A mapping company currently under contract with the Forest Service implemented the model.

4. Using these predictive maps, biometricians at the Pacific Northwest Research Station developed a recommended sampling design which included the procedures used to select the timber areas to be sampled on the ground. The sampling design was reviewed by the Region 6 Inventory Advisory Board.

5. A detailed quantitative inventory of vegetative conditions will be made in the areas identified. Under the technical supervision of the Regional Office Timber Management Inventory Sections, National Forest inventory teams will measure plots in selected areas in accordance with standard vegetative sampling and measurement procedures modified to ensure adequate sampling of Pacific yew.

6. The vegetative plot data will be compiled and analyzed to determine size and quantity distribution and will provide a vegetative data base for analyzing the Pacific yew occurrence with relation to the vegetative communities.

7. Forest Service personnel engaged in other inventories, such as stand examinations and timber cruises, have been directed to provide relevant data on the occurrence and attributes of observed Pacific yew to the Forest Service scientists conducting the National Forest Pacific yew inventories. Relevant data includes written observations and aerial photography of plot location.

8. Development of the predictive models and determination of National Forest areas to be sampled based on the predictive models were completed by the end of FY 1991. Data collection by ground surveys was initiated in FY 1991; it is anticipated that preliminary information with reasonable estimates of reliability will be available by December 31, 1991. Forest Service ground survey crews will complete any additional data collection activities by July 31, 1992. Thereafter, the Forest Service will use its best efforts to complete any necessary ground surveys, compile and analyze the inventory data, and publish

its National Forests Pacific Yew Inventories' findings by October, 1992.

9. In addition to conducting the National Forests Pacific Yew Inventories, in FY 1992 the Forest Service in the Pacific Southwest Region will conduct a limited inventory of existing Pacific yew located in portions of certain National Forests in California. This inventory will study the distribution, form class (including average diameter and range of diameters of the tree form), and vegetative communities of Pacific yew found in the inventory areas. The Forest Service may contract portions of these Pacific yew inventories.

B. <u>Conservation Biology Guidelines</u>

1. The Forest Service and the BLM will promulgate Pacific Yew Conservation Biology Guidelines (Guidelines) to provide for the sound management of the Pacific yew and associated ecosystems, to maintain the genetic diversity of the species, and to encourage yew regeneration. The Guidelines will reflect a conservation strategy derived after investigation and study of the Pacific yew. To the extent practicable, the Guidelines will utilize data from the National Forests Pacific Yew Inventories and other available data bases.

2. In FY 1991, Forest Service scientists and professionals formed a Task Force to begin developing interim Guidelines based on available data and professional knowledge specific to the Pacific yew. In promulgating these interim Guidelines, the Forest Service will conduct, to the extent practicable, retrospective field examinations of the species' response to both natural and human-caused disturbances. Additionally, the development of these interim Guidelines will include the solicitation and consideration of concerns of interest groups and parties. Target date for completion of the interim Guidelines is March 2, 1992.

3. Before promulgating revised Guidelines in later fiscal years, the Forest Service and BLM will conduct conservation biology and confirmation studies, and seek public comments on appropriate measures to include in the revised Guidelines.

C. Development of Conservation Biology Studies

1. Formal Conservation Biology studies will be initiated in FY 1992. (See Attachment 2 for a Research Proposal dated 7/9/91). Individuals responsible for developing the Conservation Biology Studies will coordinate their research protocols with members of the Pacific Yew Conservation Biology Guidelines Task Force by jointly identifying gaps in the scientific data base that must be filled prior to refining and updating these Guidelines. Conservation Biology studies will be under the direction of Forest Service scientists who hold Ph.D. degrees and who are in good standing in the scientific community.

2. The Conservation Biology studies undertaken pursuant to the Cooperative Agreement and the 1992 Plan will address two primary issues: 1) the likely impact Pacific yew harvesting will have on the long-term viability of yew growing in the wild in terms of the species' population size and distribution, and its growth and reproductive rates; and 2) the steps necessary to understand and minimize potential adverse effects of harvesting Pacific yew on the ecosystems in which it occurs.

3. Specifically, the initiated research will be conducted to evaluate the effect of harvesting on three distinct levels: individual trees and stands; the yew population as a whole; and forest ecosystems. Topics to be studied will include yew reproduction, growth and mortality, stand development, yew population size and structure, the vegetative, soil and animal components of the pertinent forest ecosystems, and other areas of research as mutually agreed upon in Annual Pacific Yew Program Plans.

4. In FY 1992, the Forest Service will initiate the yew Conservation Biology studies according to the following schedule:

Oct. - April: (a) Develop peer-reviewed study plans;
(b) hire personnel;
(c) identify cooperators and negotiate contracts; and
(d) order equipment.

March - May: (a) Hire modeler and field crews; and
(b) review existing population models.

May - Sept.: (a) Collect and enter data on all studies;
(b) begin construction of population model; and
(c) begin monitoring.

D. Pacific Yew Transfer

1. Administration

a. The Forest Service will provide the necessary personnel and administrative services to direct the transfer of Pacific yew located on National Forest lands to B-MS as agreed to in the Cooperative Agreement and Annual Pacific Yew Program Plans.

b. B-MS will name its Designated Agents in writing to the Forest Service. Designated Agents will specify in writing to the Forest Service the names, addresses, business locations, and level of authority of individuals acting as Designated Agent's Representatives, Field Supervisors, and Harvesters.

c. Pacific yew will be transferred by the Forest Service to B-MS in accordance with 16 U.S.C. § 472a(f) and other statutory and regulatory authority. All transfers will be governed by the terms of permits issued by the Forest Service. Standard and special provisions covering environmental and administrative requirements for each transfer will be attached to each permit. (See Attachment 3 for a copy of the standard environmental and administrative provisions, and Attachment 4 for a copy of special provisions.)

d. Consistent with the MOU and the Cooperative Agreement, B-MS will use Pacific yew obtained under the Annual Plan to produce taxol in accordance with its obligations under the NCI taxol CRADA. Products derived from quantities of Pacific yew transferred to B-MS cannot be used for purposes not allowed by the transfer authority.

e. B-MS, through its Designated Agents, will establish procedures requiring its Designated Agent's Representatives, Field Supervisors, and Harvesters to comply with all terms and conditions of permits or contracts transferring Pacific yew to B-MS.

f. B-MS, through its Designated Agents, will establish procedures requiring its Designated Agent's Representatives, Field Supervisors, and Harvesters to possess copies of applicable permits and other necessary documents while engaged in the harvesting, collection, and transportation of Pacific Yew pursuant to the Cooperative Agreement and Annual Pacific Yew Program Plans.

g. B-MS, through its Designated Agents, will establish procedures requiring its Harvesters to comply with all applicable environmental protection standards and permit stipulations.

h. B-MS, through its Designated Agents, will assign Field Supervisors to conduct periodic monitoring of the on-the-ground activities of Harvesters in each permit or contract area.

i. In the event that Forest Service personnel become aware of problems or violations of the terms of harvest permits by Designated Agents, Designated Agent's Representatives, Field Supervisors, or Harvesters, then a Forest Service Representative will immediately notify these parties of the problems or violations and any appropriate corrective action to be taken. The Forest Service may issue a notice of violation under 36 C.F.R. § 261 to the individual or individuals violating the terms of the permit.

If problems of a serious nature occur or violations persist or are not remedied in a timely manner, then the Forest Service may suspend operations under the applicable permit and may require whatever action is necessary to remedy the problem or violation. Initially, the Forest Service may verbally notify the appropriate Designated Agent of such problems or violations; however, the Forest Service shall promptly provide the

Designated Agent with written notification with copy to B-MS.

If problems or violations are not satisfactorily resolved after notification of the appropriate Designated Agent, then the Forest Service must provide written notification, together with a request for corrective action, to B-MS through the following individual (or her designated acting representative, supervisor, or successor):

M. Dianne DeFuria
Senior Director
Business Development & Planning
Bristol-Myers Squibb Co.
Pharmaceutical Group
P.O. Box 4000
Princeton, N.J. 08540

If satisfactory corrective action is not taken, or if the violation is serious, then the permit under which the problem or violation has occurred may be canceled by the Forest Service. In the event that the Forest Service incurs expenditures to rectify or resolve damages as a result of breach of permit stipulations by B-MS's agents, then B-MS will reimburse the Forest Service for its reasonable and necessary direct expenditures, provided that B-MS has received written notice and a request for corrective action from the Forest Service about the causative problem or violation.

j. The utilization of Pacific yew bark has two parameters: 1) the minimum size of trees and portions thereof to be peeled; and 2) an established minimum amount of bark to be stripped from trees and portions thereof designated for peeling. Utilization standards are included as Attachment 5. Attachment 5 may be amended upon mutual agreement of the parties.

If B-MS, through its Designated Agents, fails to meet Forest Service Pacific yew utilization standards, then the Forest Service may treat the failure as a violation of the terms of the permit. The Forest Service may then refuse to issue new transfers to the responsible Field

Supervisor or Harvester until harvesting under the permit meets utilization standards. Willful or repeated failures to meet utilization standards may result in the withholding of new transfers to the responsible Designated Agent's Representative, Field Supervisor or Harvester.

2. <u>Identification of Pacific Yew Available for Transfer</u>

a. The Forest Service will prioritize its FY 1992 Pacific yew bark harvest activities by evaluating potential yew harvest areas as follow:

i. Areas where yew harvest is required prior to prescribed burning within the area.

ii. Areas where yew harvest is necessary to accomplish pre-harvesting prior to the logging of other species from within harvest units of sold Timber Sale Contracts of other species.

iii. Areas already logged for other species where yew harvesting has not yet been accomplished.

iv. Areas that will be harvest units for other species in future Timber Sale Contracts with completed NEPA analyses, NEPA decisions and, where appropriate, consultation with U.S. Fish and Wildlife Service.

v. Areas that will be harvest units for other species in future Timber Sale Contracts after completion of NEPA analyses, NEPA decisions and, where appropriate, consultation with U.S. Fish and Wildlife Service.

vi. Areas where yew harvest will occur outside Timber Sale Contract harvest units for other species. Yew bark harvest will be in accordance with a prescription developed during the site specific NEPA analysis and will be consistent with interim conservation

biology guidelines. Where appropriate, consultation will be completed with U.S. Fish and Wildlife Service.

Those areas previously harvested and identified for reharvest in FY 1992 will be scheduled consistent with the above priorities.

b. In all Timber Sale Contracts sold as part of the Forest Service's annual timber program, the Forest Service will not include Pacific yew as an included species under the terms of the contract. To the extent practicable, pre-harvesting of Pacific yew will occur in harvest units of sold and future Timber Sale Contracts.

3. <u>Offer and Acceptance of Pacific Yew Available for Transfer</u>

a. The Forest Service will provide B-MS's Designated Agents with written notice of every offer to transfer yew to B-MS pursuant to the Cooperative Agreement and Annual Pacific Yew Program Plans. When immediate action is warranted, the Forest Service may provide the required notice by telephone to B-MS's Designated Agents.

b. In general, B-MS's Designated Agents will have 30 days to respond to an offer by the Forest Service to transfer Pacific yew to B-MS. However, the parties recognize that the need for immediate action occasionally may require a shorter response period; in those instances, the Forest Service will outline the nature of the immediate need and the deadline for a response date in its offer of yew for transfer to B-MS.

c. If a Designated Agent of B-MS accepts an offer for transfer of Pacific yew, Forest Service officials will issue the implementing permit, timber sale contract, or other contract in the following manner: "<u>Designated Agent</u>, acting as an agent of B-MS . . . ."

d. If B-MS's Designated Agents fail to respond to the Forest Service's offer in the specified time period, then the Forest Service may treat

the failure to respond as a rejection of the agency's offer. If B-MS's Designated Agents reject an offer for the transfer of yew, then the Forest Service may sell the yew to others.

4. <u>Compliance with NEPA, NFMA and Other Regulations and Policies</u>

   a. The Forest Service will prepare or approve all documents necessary to ensure that transfer of Pacific yew to B-MS pursuant to the Cooperative Agreement and Annual Pacific Yew Program Plans complies with applicable laws, regulations, and policies.

   b. To the extent possible, in FY 1992 Forest Service officials will offer to transfer to B-MS Pacific yew located in areas with prior existing NEPA documents. Appropriate modifications to NEPA decision documents referencing yew harvesting will be made where necessary and consistent with applicable laws, regulations, and policies.

5. <u>Programmatic Environmental Impact Statement</u>

   a. A programmatic Environmental Impact Statement (EIS) will be prepared assessing the environmental consequences of various alternatives under the Cooperative Agreement. The EIS will be prepared by a team of Forest Service specialists. The BLM and the Food & Drug Administration will be cooperating agencies in the EIS.

   b. Recognizing the need to prepare this programmatic EIS as expeditiously as possible, the Forest Service has initiated work on the document before final data from the Pacific Yew Inventories are available. Forest Service personnel responsible for conducting the inventories will coordinate with the EIS team by providing interim and final inventory data for inclusion in the EIS as expeditiously as possible. The programmatic EIS will be amended as necessary based on results from the inventories and the Conservation Biology studies. To the extent practicable, the EIS will address issues of interest to other agencies, including the BLM and the Food & Drug Administration.

c. Consistent with the critical nature of the programmatic EIS, on September 30, 1991, the Forest Service published in the Federal Register a Notice of Intent announcing the decision to prepare a programmatic EIS. The Forest Service will undertake those activities necessary to complete the EIS, including scoping, preparation of a draft EIS, solicitation and consideration of public comments, and preparation and publication of a final EIS.

d. Pending completion of the programmatic EIS, all Pacific yew harvests will be covered by site specific environmental analysis and supported by appropriate NEPA documentation. As appropriate, Pacific yew harvests will comply with the Endangered Species Act.

6. <u>Accounting for Pacific Yew</u>

a. B-MS, through its Designated Agents, will accept Pacific yew only when accompanied by documentation granting permission to harvest. B-MS, through its Designated Agents, will keep records of all Pacific yew transactions. Records will include the following information:

a) date of transaction;
b) name and address of person delivering Pacific yew;
c) vehicle license number;
d) land owner's name and address;
e) harvest site and, as applicable, the Permit Number;
f) quantity of Pacific yew delivered; and
g) proof of authorization to harvest, as established in a permit or other document granting such permission.

b. B-MS, through its Designated Agents, will cooperate fully with the Forest Service in conducting law enforcement investigations pertaining to Pacific yew. Such cooperation shall include granting access to yew harvest records necessary for the conduct of law enforcement investigations.

B-MS will also cooperate fully with the Forest Service by granting access to yew harvest

records necessary to complete mandated environmental analyses.

c. B-MS, through its Designated Agents, will maintain records of yew acquired under the Cooperative Agreement. Records will include the following information about each permitted transfer:

a) National Forest;
b) Ranger District;
c) name of permitted area, permit number, and permit termination date;
d) Forest Service estimate of Pacific yew to be transferred;
e) the weight of yew delivered by Field Supervisor;
f) the date of the delivery; and
g) the name and address of the Designated Agent's Representatives, Field Supervisors, and Harvesters acting under each permit.

d. B-MS's Designated Agents will provide each National Forest with weekly summaries by permit and by Harvester of Pacific yew collected under Forest Service permits. The weekly summaries will be forwarded each Monday afternoon to Ranger District and National Forest Pacific Yew Coordinators designated by the Forest Service.

e. B-MS's Designated Agents will also provide a monthly accounting which will include the information in paragraph d., above. The monthly accounting will be forwarded to each Ranger District and National Forest Pacific Yew Coordinator within 15 days of the end of the preceding month with copies to the appropriate Regional Office Coordinators.

V. Harvesting Goals

A. In General

1. The FY 1992 goal for yew collection/harvesting for B-MS pursuant to the Cooperative Agreements and 1992 Plans is at least 750,000 pounds of dried bark from Pacific Yew located on lands under the control of either the Forest Service or the BLM. Under the terms of the Cooperative Agreement and 1992 Plan

between B-MS and the Forest Service, the Forest Service agrees to make Pacific yew available, in accordance with all applicable laws, regulations and policies, to meet this 1992 harvesting goal for Pacific yew located on federal lands.

B. Limits on Pacific Yew Harvesting by Third Parties

1. The Forest Service and B-MS recognize the need to ensure that legitimate efforts by parties other than B-MS to produce taxol for use in humans be allowed to proceed. On the other hand, the realities of current taxol sourcing, and the government-wide commitment to cooperating with the NCI's CRADA partner, dictate that reasonable limits be placed on third parties' harvesting of Pacific yew located on federal lands.

2. The FY 1992 limit for transfer of Pacific yew located in the National Forests to parties other than B-MS is 10,000 pounds of dried Pacific yew bark per research project, and 50,000 pounds of dried Pacific yew bark overall, for use in the research or development of taxol for use in humans.

3. Until further notice from B-MS, there is no limit on the amount of Pacific yew needles or other foliage that can be transferred from the National Forests to parties other than B-MS for use in the research or development of taxol for use in humans. The parties acknowledge that B-MS may amend this policy during the term of the 1992 Annual Plan.

4. The parties agree that if B-MS cannot practicably utilize Pacific yew transferred by the Forest Service for purposes consistent with the NCI CRADA, then the Forest Service may sell this Pacific yew to other parties. Yew sold to other parties under these circumstances is not subject to the conditions specified in Paragraphs 2 and 3, above.

VI. Funding

A. Funding Levels

1. In FY 1992, B-MS will provide the Forest Service with adequate amounts to support the programs and activities outlined in the Cooperative Agreement

and the 1992 Plan; without B-MS's prior written approval, this amount will not exceed the funding level identified in Schedule A of the Cooperative Agreement. The parties acknowledge that the sum in Schedule A is an estimate which could be subject to change depending on circumstances beyond the control of either party, including unexpected costs associated with preparing a programmatic EIS, court orders, and legal challenges. The sum in Schedule A reflects costs associated with implementing the Cooperative Agreement in Regions 1 and 6.

2. In FY 1992, B-MS will make an initial deposit to the Pacific Yew Account in accordance with Schedule 1 within 15 days following the execution of the 1992 Plan. Additional deposits to cover other costs incurred with regard to the FY 1992 Program Elements will be based on estimates supplied by the Forest Service and remitted by B-MS in advance and on a quarterly basis.

3. The funds in the Pacific Yew Account will be allocated in accordance with a document entitled "Pacific Yew Direct and Indirect Costs Estimate 2/4/92," and attached hereto as Schedule 1. B-MS will not be obligated to submit funds in excess of the amounts designated in Schedule 1 unless the Company, in its sole discretion, agrees to do so, pursuant to Paragraph 4.

4. It may become apparent to Forest Service personnel that the Pacific Yew Account does not contain sufficient funds to complete the agency's obligations for FY 1992, as outlined in the Cooperative Agreement and the 1992 Plan. In this event, the Forest Service will provide B-MS with its estimate of the additional funds needed, and a description of the activities to be completed with these funds. B-MS will have the sole right to decide whether to remit additional sums to the Forest Service to support the specified activities. The Forest Service and B-MS will mutually agree upon how to allocate the remaining funds among the FY 1992 Program Elements if B-MS elects not to remit additional funds to the Pacific Yew Account.

B. <u>Accounting Procedures</u>

1. The Forest Service will establish a special account known as the Pacific Yew Account. B-MS will remit

the funds called for under the Cooperative Agreement and the 1992 Plan to the Pacific Yew Account. To the extent possible, the Forest Service will distribute these funds according to Schedule 1 of the 1992 Plan.

2. The Forest Service will provide B-MS with an estimate of yew program expenses by the 20th of the month preceding the beginning of each quarter. These estimates will be reduced by any unexpended funds that remain in the Pacific Yew Account after the end of the prior operating quarter. If provided with a timely estimate of yew program expenses, then B-MS will make payment within twenty days after the beginning of the quarter. Otherwise, B-MS will remit payment with thirty days of receipt of the Forest Service's estimate of yew program expenses.

3. Accounting for actual year-to-date costs will be completed by the Forest Service and provided to B-MS by the 30th of the month following the end of each operating quarter. The quarterly accounting statements will present the current balance for the Pacific Yew Account and itemize deposits to and expenditures from the Account. These accounting statements will include a breakdown by region of the costs associated with each Program Element, a brief description of the services or goods purchased with the expended sums, an entry for indirect or overhead costs, the total expenditures for the quarter, and other information as agreed upon by the Forest Service and B-MS. Additionally, the Forest Service will provide B-MS with documents verifying the itemized expenditures from the Pacific Yew Account.

/s/ Zola Horovitz

Zola Horovitz, Ph.D.
Vice President, Business
Development and Planning
Bristol-Myers Squibb Company

/s/ John E. Lowe for

John F. Butruille
Regional Forester
Region 6
USDA Forest Service

/s/ David M. Spores for

David F. Jolly
Regional Forester
Region 1
USDA Forest Service

Presidential Documents

Executive Order 12600 of June 23, 1987

Predisclosure Notification Procedures for Confidential Commercial Information

By the authority vested in me as President by the Constitution and statutes of the United States of America, and in order to provide predisclosure notification procedures under the Freedom of Information Act concerning confidential commercial information, and to make existing agency notification provisions more uniform, it is hereby ordered as follows:

Section 1. The head of each Executive department and agency subject to the Freedom of Information Act shall, to the extent permitted by law, establish procedures to notify submitters of records containing confidential commercial information as described in section 3 of this Order, when those records are requested under the Freedom of Information Act (FOIA), 5 U.S.C. 552, as amended, if after reviewing the request, the responsive records, and any appeal by the requester, the department or agency determines that it may be required to disclose the records. Such notice requires that an agency use good-faith efforts to advise submitters of confidential commercial information of the procedures established under this Order. Further, where notification of a voluminous number of submitters is required, such notification may be accomplished by posting or publishing the notice in a place reasonably calculated to accomplish notification.

Sec. 2. For purposes of this Order, the following definitions apply:

(a) "Confidential commercial information" means records provided to the government by a submitter that arguably contain material exempt from release under Exemption 4 of the Freedom of Information Act, 5 U.S.C. 552(b)(4), because disclosure could reasonably be expected to cause substantial competitive harm.

(b) "Submitter" means any person or entity who provides confidential commercial information to the government. The term "submitter" includes, but is not limited to, corporations, state governments, and foreign governments.

Sec. 3. (a) For confidential commercial information submitted prior to January 1, 1988, the head of each Executive department or agency shall, to the extent permitted by law, provide a submitter with notice pursuant to section 1 whenever:

(i) the records are less than 10 years old and the information has been designated by the submitter as confidential commercial information; or

(ii) the department or agency has reason to believe that disclosure of the information could reasonably be expected to cause substantial competitive harm.

(b) For confidential commercial information submitted on or after January 1, 1988, the head of each Executive department or agency shall, to the extent permitted by law, establish procedures to permit submitters of confidential commercial information to designate, at the time the information is submitted to the Federal government or a reasonable time thereafter, any information the disclosure of which the submitter claims could reasonably be expected to cause substantial competitive harm. Such agency procedures may provide for the expiration, after a specified period of time or changes in circumstances, of designations of competitive harm made by submitters. Additionally, such

procedures may permit the agency to designate specific classes of information that will be treated by the agency as if the information had been so designated by the submitter. The head of each Executive department or agency shall, to the extent permitted by law, provide the submitter notice in accordance with section 1 of this Order whenever the department or agency determines that it may be required to disclose records:

(i) designated pursuant to this subsection; or

(ii) the disclosure of which the department or agency has reason to believe could reasonably be expected to cause substantial competitive harm.

Sec. 4. When notification is made pursuant to section 1, each agency's procedures shall, to the extent permitted by law, afford the submitter a reasonable period of time in which the submitter or its designee may object to the disclosure of any specified portion of the information and to state all grounds upon which disclosure is opposed.

Sec. 5. Each agency shall give careful consideration to all such specified grounds for nondisclosure prior to making an administrative determination of the issue. In all instances when the agency determines to disclose the requested records, its procedures shall provide that the agency give the submitter a written statement briefly explaining why the submitter's objections are not sustained. Such statement shall, to the extent permitted by law, be provided a reasonable number of days prior to a specified disclosure date.

Sec. 6. Whenever a FOIA requester brings suit seeking to compel disclosure of confidential commercial information, each agency's procedures shall require that the submitter be promptly notified.

Sec. 7. The designation and notification procedures required by this Order shall be established by regulations, after notice and public comment. If similar procedures or regulations already exist, they should be reviewed for conformity and revised where necessary. Existing procedures or regulations need not be modified if they are in compliance with this Order.

Sec. 8. The notice requirements of this Order need not be followed if:

(a) The agency determines that the information should not be disclosed;

(b) The information has been published or has been officially made available to the public;

(c) Disclosure of the information is required by law (other than 5 U.S.C. 552);

(d) The disclosure is required by an agency rule that (1) was adopted pursuant to notice and public comment, (2) specifies narrow classes of records submitted to the agency that are to be released under the Freedom of Information Act, and (3) provides in exceptional circumstances for notice when the submitter provides written justification, at the time the information is submitted or a reasonable time thereafter, that disclosure of the information could reasonably be expected to cause substantial competitive harm;

(e) The information requested is not designated by the submitter as exempt from disclosure in accordance with agency regulations promulgated pursuant to section 7, when the submitter had an opportunity to do so at the time of submission of the information or a reasonable time thereafter, unless the agency has substantial reason to believe that disclosure of the information would result in competitive harm; or

(f) The designation made by the submitter in accordance with agency regulations promulgated pursuant to section 7 appears obviously frivolous; except that, in such case, the agency must provide the submitter with written notice of any final administrative disclosure determination within a reasonable number of days prior to the specified disclosure date.

Sec. 9. Whenever an agency notifies a submitter that it may be required to disclose information pursuant to section 1 of this Order, the agency shall also notify the requester that notice and an opportunity to comment are being

provided the submitter. Whenever an agency notifies a submitter of a final decision pursuant to section 5 of this Order, the agency shall also notify the requester.

Sec. 10. This Order is intended only to improve the internal management of the Federal government, and is not intended to create any right or benefit, substantive or procedural, enforceable at law by a party against the United States, its agencies, its officers, or any person.

Ronald Reagan

THE WHITE HOUSE,
June 23, 1987.

[FR Doc. 87-14602
Filed 6-23-87; 4:38 pm]
Billing code 3195-01-M

United States Department of Agriculture | Forest Service | Pacific Northwest Research Station | P.O. Box 3890
Portland, Oregon 97208

Reply To: 1620

Date: July 9, 1991

Dianne DeFuria
Director, Licensing
Bristol-Myers Squibb
Pharmaceutical Group
P.O. Box 4000
Princeton, N.J. 08540

Dear Ms. DeFuria:

Enclosed is a proposal for research that the Pacific Northwest Research Station would undertake under the cooperative agreement between the USDA Forest Service and Bristol-Meyers Squibb Company.

We would like this to be the document used in developing the research portion of the 1992 Annual Pacific Yew Program Plan.

Sincerely,

/s/ Sally Sullivan (for)
CHARLES W. PHILPOT
Station Director

Enclosure

cc: with enclosure
Peyton Owston, CFSL
Robert J. Devlin, R-6 Timber Management
Fred Page, R-6 Timber Management

Authored:D.Minore 7/2/91Reviewed:P.Owston 7/2/91Reviewed:S.Till 7/2/91Reviewed:A.Walker:07/08/91

Attachment 2

PROPOSAL FOR RESEARCH ON THE CONSERVATION OF PACIFIC YEW POPULATIONS

The proposed harvesting of large quantities of Pacific Yew bark requires research on the population viability of the species under different levels of harvesting and the potential effects of harvesting on the forest ecosystem. That research will require a thorough knowledge of species biology, and the biology of Pacific yew is not well understood. Three critical factors make it desirable to accomplish the work outlined in this proposal:

<u>1. The Viability of Wild Populations</u> There is a small but significant risk to the continued viability of many subpopulations of yew within its range and a risk of significant alteration of the yew population throughout its range if exploitation were to continue at high levels for long periods of time. Although it is expected that the need to utilize the bark of wild populations will decline significantly in the next 3-5 years, the foliage of wild yew trees may be needed for many years. The extremely low level of scientific information about yew population sizes and distributions, yew growth and reproductive rates, and yew ecology make potential impacts of continued yew harvest uncertain.

<u>2. The Continued Availability of Yew Bark</u>. There is a significant risk that legal and political limitations will make it difficult to sustain continued production of Yew bark from wild populations. The current social sensitivity to the impacts of forestry on biological diversity, spotted owls, and old growth has greatly affected the kinds and levels of acceptable resource production from forests; and these same issues are often associated with Pacific yew. Although the risks of adverse ecological impacts from harvesting of yew may be small, the burden of proof has shifted from those who want to protect the environment to those who want to extract products from it. In the current forest management crises in the Pacific Northwest, opportunities to obtain Pacific Yew as a by-product of timber production may drop dramatically as the level of timber cutting in mature and old-growth forests declines. If that happens future harvests of yew bark would have to come increasingly from intact mature and old- growth stands, which could be an extremely sensitive issue. The lack of basic ecological information about the species and its role in the ecosystem increases the likelihood that limitations may be placed on the exploitation of yew under the justification that information does not exist to develop adequate environmental impact assessments.

<u>3. The Ecostystem</u> Pacific yew is a scattered small tree in a vast and complex forest ecosystem. It is, however, ecologically distinctive in several respects including animal-dispersed seeds, foliage that is highly palatable to ungulates, and unique chemical characteristics of its tissues (roots, bark and foliage). The attributes of Pacific Yew that give it medicinal qualities may also make it valuable to organisms that utilize its roots, fruits, and foliage for food and resources. Perhaps the greatest risk of impact on the ecosystem from the harvesting of yew trees comes from the harvesting activities themselves. Adverse affects on soil, behavior of other organisms, and stream ecosystems are possible from harvesting activities.

OVERALL OBJECTIVES OF THE RESEARCH PROGRAM

The general objective of the research program will be to assess factors 1 and 3 above and compile scientifically sound information to aid in predicting and/or minimizing the probability that legal challenges and social pressures will restrict the availability of yew products from the National Forests.

The research effort will consist of three parts: Effects on individual yew trees and stands, effects on yew populations, and effects on forest ecosystems.

EFFECTS ON INDIVIDUAL YEW TREES AND STANDS

Reproduction

Maintenance of vigorous, viable yew populations depends upon prompt, efficient replacement of the trees removed during harvest. Natural regeneration would best conserve local gene pools and accomplish this replacement in harmony with local ecosystem processes, but planting should also be utilized when needed. Both sexual and asexual regeneration are involved, and both should be studied to assure success. Answers to the following questions should be obtained through replicated measurement and experimentation:

1. What is the relative importance of sexual and asexual reproduction under both natural and disturbed conditions?
2. What sex ratios occur in nature, and what is the optimal female/male ratio for abundant seed production in the female trees?
3. What environmental conditions (light, temperature, moisture, nutrients) are most favorable for seed production?
4. How are yew seeds dispersed in nature, and how far do they travel from the parent tree?
5. What moisture, temperature, light, and seedbed conditions are optimal for seed stratification, germination and initial seedling establishment, and what is the physiological nature of seed dormancy?
6. How fast do seedlings grow, and what environments (light, temperature, moisture, nutrients) result in maximum growth? How large and in what physiological condition should cuttings or seedlings be to best utilize those environments?
7. Are seedling establishment, growth, and mortality functions of stand conditions? If they are, what are the effects of yew tree harvest on those conditions, and how does that harvest affect other species in the stand?
8. Will yew stumps produce sprouts that develop into vigorous trees capable of replacing those that were cut? If so, what are the optimal stump heights, seasons of cutting, and sprout locations for such development?

9. What percentage of the harvested yew trees must be replaced through artificial regeneration to maintain genetic diversity and a viable population?

The first two questions will be answered by conducting extensive field surveys in areas where Pacific yew is abundant. Question 3 will be answered by analyzing the microclimate of individual fruiting trees and by relating good seed years to local meteorological records. Field observations, stomach and crop analyses, and seed labelling experiments will be used to answer the fourth question. Questions 5 and 6 will be anwswered by subjecting seeds and seedlings to controlled growth chamber and greenhouse conditions and by using the results to select suitable field environments. Replicated planting studies will be established in both undisturbed stands and stands where yews have been harvested, and carefully measured stand characteristics will be related to the results to obtain answers to question 7. Replicated stump-height and bark-condition experiments will be established in several seasons to answer question 8. Question 9 will be answered by studying the gene pool and natural regeneration on a variety of sites.

<u>Growth and Mortality</u>

Pacific yew is a slow-growing species, but growth data are scarce, and actual growth rates for specific environmental conditions and levels of competition are unknown. The species is thought to be long-lived, but maximum ages are not available; and the interactions of growth rate, environment, and longevity are obscure. The effects of yew utilization and stand disturbance on growth and mortality could have profound effects on Pacific yew populations. If native Pacific yew is to be conserved, more must be known about the growth, life, and death of the individual trees that make up those populations:

1. What environmental conditions (light, temperature, moisture, nutrients) result in maximum growth of Pacific yew, and what constitutes an optimum yew site?
2. How do stand conditions (both disturbed and undisturbed) affect yew growth and mortality, and how will yew harvest affect those conditions?
3. What are the effects of yew age on growth and mortality?
4. Can bark be harvested from mature yew trees without killing those trees? If so, how? How much bark can be taken, and how should the bark that is left be distributed?
5. How do understory yew trees respond when exposed to full sunlight after stand disturbance removes the overstory? Will growth be better or worse after the trees adapt to this extreme change? What light conditions are best for branch growth?
6. How does branch and needle removal affect the survival, growth, and needle production of mature yew trees?
7. How are yew growth and mortality affected by vegetative competition, and how can these effects be quantified to predict yew response when competition increases or decreases?

Question 1 will be answered by the measurement and instrumentation of at least five sites that support vigorous yew growth. Measurement of stand composition, age, and density will be related to tree, shrub, and herb growth on both undisturbed and disturbed sites in answering question 2. Question 3 will be answered by determining age, growth rate, and mortality in many Pacific yew trees, on a variety of sites. The fourth question will be answered by establishing partial-bark-removal experiments with three-to-five treatments replicated on a variety of sites. Questions about response to exposure (item 5) will be answered by retrospective study and measurement of residual yew trees exposed in clearcut areas of known age. Replicated shearing treatments will be employed to answer question 6. A combination of retrospective studies of yew growth under various vegetative conditions and controlled, replicated vegetation removal experiments will be used to answer question 7.

Stand Development

Information about how relatively dense stands of yew became established in natural stands and in previously logged stands will be useful in determining conditions that promote the establishment and growth of local subpopulations of yew. In addition, information about yew distribution and growth relative to canopy gaps, soil disturbance and dense closed canopy areas will provide valuable information on how within-stand harvesting of yew trees will affect the future structure of subpopulations of yew:

1. When and how do yews become established in undisturbed, "natural" stands?
2. When and how do yews become established in disturbed stands that have been harvested for timber or yew bark?
3. How do yew abundance and density vary with stand age and density?

All three of these questions will be answered by restrospective study of existing stands (both undisturbed and disturbed). Existing trees will be aged, stand histories reconstructed, and successional trends examined.

Assignment of Personnel

Don Minore (Pacific Northwest Research Station) and Nan Vance (Pacific Northwest Research Station) will lead the ecological and physiological studies of individual yew trees and stands. Most of the actual research will be accomplished by qualified research assistants, technicians, or graduate students that will work under Minore's or Vance's supervision. The research will be headquartered in Corvallis, Oregon, but field work will be accomplished in the Oregon and Washington Cascade Range where Pacific yew is abundant.

Estimated Costs

Scientist/professional salaries	$165,000
Technician/graduate student support	95,000
Travel	21,000
Equipment, services, and supplies	32,000
Total	$313,000

EFFECTS ON YEW POPULATIONS

A conservation biology perspective will be used to assess the potential effects of different levels of yew harvesting on yew populations and to recommend management strategies that will conserve the species while providing yew products. To accomplish this a population viability approach (PVA) will be taken. PVA is a conceptual or mathematical model of a population of organisms that assesses population levels over time as a function of mortality rates, growth rates, reproductive rates, and habitat distribution and loss. Once such a model is developed, effects on populations of different levels of exploitation can be assessed in simulations. Information needed to develop such a model and assess potential impacts of different management intensities consists of the following:

1. Size or age-specific mortality/survival rates in different environments such as clearcuts, young forests, old forests. (See "Growth and Mortality" - questions 2,3, and 7 above).
2. Transition rates (taking into account growth and mortality) from one size/age class into another for different envionments. (See "Stand Development" above).
3. Current population size and structure estimates for different environments
4. Fecundity rates by size/age classes for different environments. (See "Reproduction" - question 3 above).
5. Locations and maps of Yew populations and potential habitats across the landscape
6. Dispersal distances in the managed landscapes. (See "Reproduction" - question 4 above).

Assignment of Personnel

The population effects portion will be under the supervision of Thomas Spies, Pacific Northwest Research Station. Spies will hire a Postdoctoral scientist who will conduct much of the research and modelling. A data analyst will be hired to assist the postdoc and temporary field crews will be hired to characterize the structure of existing Yew populations.

Estimated Costs

Scientist/professional salaries	$192,000
Technician/graduate student support	95,000
Travel	20,000
Equipment, services, and supplies	9,000
Total	316,000

EFFECTS ON FOREST ECOSYSTEMS

Many potential effects of yew harvesting on the ecosystem could be examined. We take the position that priority should be given to yew population and biology studies because the ecological impacts will be most direct on the species itself. Consequently, some priorities must be set for the ecosystem effects studies. The top priority research areas are: effects on other organisms of reductions in yew populations, and effects of harvesting practices on other organisms and the environments of closed canopy forest stands.

To evaluate potential effects on other organisms of reductions in yew populations, information is needed on associations between yew and other organisms. These associations fall into several categories:

1. The association of understory vegetation and soil flora and fauna with mature yew trees and stands with high yew densities. To meet this objective surveys of vegetation, soil organisms and chemical properties will be conducted under yew trees and under randomly chosen locations in forests. The hypothesis will be tested that soils under yew trees do not differ from randomly chosen forest soils in either species composition or chemical characteristics.
2. Herbivore associations with yew foliage. Invertebrate and vertebrate surveys of herbivores that feed on yew foliage will be made. Chemical analysis of nutrient quality and quantity of yew foliage will be made in different environments.
3. Organisms that feed on yew fruits. Surveys will be made for organisms that feed on yew fruits and disperse yew seeds. The chemical and energetic quality of yew fruits will be evaluated and yew's contribution to the total fruit production of a forest assessed.
4. Effects of harvesting practices on intact forest ecosystems. This research project will be conducted through synthesis of existing information and consulations with spotted owl biologists and stream ecologists.

Assignment of Personnel

The ecosystem effects research will conducted by several cooperators who will be supervised by Spies and Minore. Scientists from the U.S. Forest Service and Oregon State University will be contracted to conduct much of the ecosystem research. Monitoring will be conducted by U.S. Forest Service National Forest System personnel.

Estimated Costs

Scientist/professional salaries	$45,000
Technician/graduate student support	164,000
Travel	15,000
Equipment, services, and supplies	25,000
Total	249,000

Estimated Total Cost of Entire Research Effort: $878,000

RESEARCH PRODUCTS

In addition to scientific publications the following research products will be made available:

1. Preliminary report on population impacts of different levels and types of yew utilization. End of Year 2
2. Final report on probable impacts of different levels, types and durations of yew harvesting on population levels. End of Year 3
3. Final report on probable effects of yew harvesting on selected components of the yew ecosystem. End of Year 3
4. Final reports on guidelines for maintenance of yew populations through natural and artificial regeneration methods

Spies and Minore will be responsible for preparing these products. The initial report (item 1) will summarize the past and present effects of yew utilization. Subsequent reports (items 2 and 3) will apply those effects to future yew populations and yew ecosystems under several possible scenarios. Final guidelines (item 4) will be based on silvicultural techniques that best satisfy the ecological, environmental, and genetic attributes of Pacific yew populations presented in items 1-3.

Attachment 2

RESEARCH SCHEDULE

Most research will be conducted and completed within three and one-half years. Monitoring will be conducted over a five-year period or less depending on levels and projections of harvesting.

FY 92

Oct-March:	Develop detailed study plans Hire Personnel Identify cooperators and set up contracts Order equipment
March-May:	Identify field study locations Hire field crews Review population models
May-Sept:	Conduct field work on all phases Begin construction of population model Begin monitoring

FY 93

Oct-March:	Enter data Conduct prelimary analyses Evaluate effects of harvesting with preliminary model
April-Sept:	Continue field work on all phases Prepare report on prelimary population models Complete field studies of ecosystem effects Continue monitoring

FY 94

Oct-March:	Analyze ecosystem effect data, prepare preliminary reports Analyze tree, stand, and population data, prepare preliminary reports Reparameterize the population model by using field data Continue monitoring
April-Sept:	Complete all field research efforts

FY 95

Oct-March:	Prepare and complete final reports Prepare journal articles
March:	End Research projects

FY 95-97	Continue montoring of populations after harvest as needed Prepare report on monitoring results

_______________ **NATIONAL FOREST**
_______________ **RANGER DISTRICT**

ADMINISTRATIVE USE PERMIT - YEW HARVEST
Ref:36 CFR 223.2(C), FSM 2463.02 -- 5/5/92

Permission is hereby granted:	Hauser Northwest, Inc. Acting as an Agent for Bristol Myers-Squibb 78120 Highway 99 South Cottage Grove, OR 97424	Permit #_______________ Date Issued: ___________ Termination Date:________ Extended to: ___________

Represented by:

_____________________________ & _____________________________
Designated Agent's Representative — Field Supervisor
_____________________________ _____________________________
_____________________________ _____________________________
Ph:_______________ Ph:_______________

THE PURPOSE for this transfer is to harvest and remove bark and other parts from Pacific yew (Taxus brevifolia) from the National Forest lands described below. The transfer of Pacific yew is provided for in THE COOPERATIVE AGREEMENT between BRISTOL-MYERS SQUIBB, CO., and USDA FOREST SERVICE, dated 6/19/91. This transfer is subject to all the terms and conditions of the Cooperative Agreement, all subsequent amendments, and the ANNUAL PACIFIC YEW PROGRAM PLAN, and to the provisions attached hereto.

DESCRIPTION OF PACIFIC YEW (Specify product; estimated bark weight, number of posts or measure of other products. Identify means of designation. Include or refer to any special cutting or harvesting prescriptions.)

UTILIZATION SPECIFICATIONS: Unless specified below, all stems with a large end or stump diameter of 3" or larger shall have all bark from stems and branches down to a 1 inch small end diameter removed from the Permit Area and delivered to the agreed upon Delivery Point.

DESCRIPTION OF LANDS FROM WHICH PACIFIC YEW WILL BE TAKEN (Include legal description of area. Include map of the location, name and extent of area(s).

Delivery Point: _______________________________
Haul Route by Road Numbers: _______________________________
Pacific Yew Trip Ticket #: _______________________________
Vehicle Identification: _______________________________

Both Forest Service and Permittee agree this product is acquired at a cost less than established fair market value. The word cost means face, par or market value, or price, either wholesale or retail, which ever is greater.

In consideration of such permission I agree to -

1. Harvest only such Pacific yew as is designated by a Forest Officer.
2. Remove no Pacific yew product until permission is given.
3. Conduct the harvesting and dispose of the refuse as directed by the Forest Officer.
4. Comply with the TERMS and CONDITIONS listed in all provisions and other attachments to this Permit.
5. Comply with all other regulations governing National Forests.
6. Conduct operations in a workmanlike and orderly manner, with a timely completion of any harvest area entered.

I understand and agree that cutting or taking any material under this Permit makes all the conditions binding. I further understand that the Code of Federal Regulations, Part 261, pertain to the Permit and that violations of this Permit may be prosecuted thereunder.

Accepted by:______________________________Date:____________
Designated Agent/Representative

Approved by:______________________________Date:____________
Authorized Forest Officer

STANDARD PROVISIONS
TO ADMINISTRATIVE USE PERMITS
TO BE APPLIED WHEN APPROPRIATE AS DETERMINED BY B-MS'S OPERATION
OUTLINED IN EACH TRANSFER PERMIT

STANDARD CONDITIONS [Items 8 thru 15 are Standard 2400-3 CONTRACT Provisions]

1. Transfer of Title - Title of all Pacific yew products included in this permit shall remain in the United States until it has been harvested; counted, measured or weighed; and leaves the National Forest.

2. Measuring of Products - Bark is to be field weighed prior to removal from the Permit Area using scales approved by the Forest Service; other products are to be counted, measured or tallied in a manner approved by the Forest Service prior to removal from permit area.

3. Authorization - Any individual, while harvesting, transporting or otherwise handling Pacific yew under the terms of this permit shall have a document in their possession authorizing them to do so; or be under the immediate supervision of an individual who posesses such an authorization, is delegated supervisory authority, and is present in the immediate area of the activity.

4. Pacific Yew Removal Receipts: Any individual harvesting, transporting or otherwise handling Pacific yew under the terms of this permit shall utilize the five part serially-numbered Pacific Yew Trip Ticket for the transportation and accounting of the yew harvested by this permit.

--Part E shall be used as a haul permit, shall contain a field measurement of the quantity removed and will be displayed at the back of the load.

--Part A shall contain a field measurement of the quantity removed and will be returned to the Forest Service office from which it was issued or deposited at a location designated by the Authorized Officer.

--Part B contain both the field measurement of the quantity removed and the certified measurment of the product as recorded into the inventory of the agent and will be returned to the Forest Service office from which it was issued.
--Parts C and D are agents' reciepts for inventory management.

If and when the Pacific Yew Trip Ticket are not available, serially-numbered Forest Products Removal Receipts may be used.

The Forest Products Removal Receipts shall contain:

1. Product description (bark, bole, needles, etc.);
2. Quantity being removed, (bark by field weight, other products by a method of measurement approved by the Forest Service;
3. Unit of measure (pound, lineal foot, number, etc.)
4. Permit number;
5. Issuing Forest Service office;
6. Name and original signature of Field Supervisor.

7. Date and time of removal from Permit Area;
8. Haul vehicle description;
9. Haul vehicle license number;
10. Gross weight; and,
11. Name of Harvester.

ATTACHMENT 3 PAGE 3

5. <u>Conduct of Operations</u> - B-MS shall conduct all operations under this permit in a safe, workmanlike manner, and shall minimize soil erosion and damage to young growth or trees left standing, and take all reasonable precautions to prevent pollution of air, soil, and water.

Unless otherwise agreed to in writing, stumps height shall not exceed 16 inches or be less than 10 inches, and will have bark intact to promote sprouting.

Any stem or portion of tree which is to be utilized for bark that can meet the wood utilzation storage standards of being eight feet in length to a small end diameter of 4 inches will not be bucked below the 4 inch top unless bucking can be done in multiples of eight feet or longer.

When specific methods of skidding or yarding are required, their location will be shown on a Permit Area map.

Where shown on a Permit Area Map, wheeled or track-mounted equipment is prohibited unless otherwise agreed to in writing.

Unless otherwise agreed to in writing, transportation of Pacific yew harvested under this permit will occur only on the haul route identified as described or shown on the Permit Area Map.

Unless otherwise agreed to in writing, harvesting and transporting of Pacific yew will be confined to daylight hours.

6. <u>Harvest of Yew in Riparian Areas</u> - Riparian Areas which are subject to this provision are shown on a Permit Area map. Unless otherwise noted on the Permit Area Map, harvest of yew will not take place within 75 feet (slope distance) from the average high water level of a perennial stream.

7. <u>Use of Premises, Camps</u> - Before any camp is set up on lands administered by USDA Forest Service, B-MS or their Agent shall obtain written permission through the District Ranger. A camp is interpreted to include a campsite or trailer parking area of any individual working on this permit for B-MS.

8. <u>Conduct of Logging in Critical Multiple-Use Areas</u> - In areas designated as "Modified Logging Area" on a Permit Area Map, the following measures are applicable unless other methods or requirements are agreed to in writing between B-MS and Forest Service.

(a) Nonspecified roads, skid roads and landings shall be located on the ground and approved by Forest Service prior to construction or the felling of adjacent timber.

(b) Felled or windthrown timber that must be disturbed in construction of roads, skid roads or landings shall be bucked prior to moving if necessary to minimize disturbance to forest values.

(c) Trees shall be felled and skidded in such a manner as to minimize disturbance to surrounding forest values.

(d) Limbs that may do damage to forest values shall be severed prior to skidding.

(e) Use of tractors shall be restricted to skid roads and other approved cleared areas.

(f) Landing size will be held to a minimum.

(g) Skidding shall be away from existing roads, trails, water sources, streamcourses and occupancy areas.

9. <u>Protection, Use and Maintenance of Improvements</u> - B-MS, in all phases of harvest operations, shall protect, insofar as practicable, all land survey corners, telephone lines, ditches, fences and other improvements. If such improvements are damaged by B-MS's operations under this permit, B-MS shall restore them immediately to condition existing immediately prior to damage. All roads and trails designated by Forest Service as needed for fire protection or other purposes, shall at all times be kept free of logs, brush, and debris resulting from B-MS's operations. Roads or trails damaged shall promptly be restored by B-MS.

B-MS use of existing roads may be restricted when indicated on a Permit Area map.

10. <u>Streamcourse Protection</u> - Streamcourses which are subject to this Provision are shown on a Permit Area map. Unless otherwise agreed, the following measures shall be observed to protect streamcourses.

(a) Operations shall be conducted to prevent debris from entering streamcourse. In event B-MS operation causes debris to enter streamcourses in amount which may adversely affect the natural flow of the stream, water quality or fishery resource, B-MS shall remove such debris as soon as practicable, but not to exceed 48 hours, and in an agreed manner that will cause the least disturbance to streamcourses.

(b) Culverts or bridges shall be required on temporary roads at all points where it is necessary to cross streamcourses with mechanized equipment. Such facilities shall be of sufficient size and design and installed in a manner to provide unobstructed flow of water and to minimize damage to streamcourses. Trees or products shall not be otherwise hauled or yarded across streamcourses unless fully suspended.

(c) Wheeled or track-laying equipment shall not be operated in streamcourses except at crossings designated by Forest Service or as essential to construction or removal of culverts and bridges.

11. <u>Landings, Roads, and Skid Trails</u> - Landings, roads and skid trails to be used shall be agreed upon prior to their use; and improvements on existing facilities shall not exceed that needed for safe and efficient operations.

Slash, stumps or other debris resulting from improvement of facilities shall be treated or disposed of as slash unless agreed otherwise.

After landings have served B-MS's purpose, B-MS shall ditch or slope them to permit water to drain or spread. Unless agreed otherwise, cut and fill banks around landings shall be sloped to remove overhangs and otherwise minimize erosion.

ATTACHMENT 3 PAGE 5

After a temporary road or skid trail has served B-MS's purpose, B-MS shall remove bridges and culverts, eliminate ditches, outslope roadbed, remove ruts and berms, effectively block the road to normal vehicular traffic where feasible under existing terrain conditions and build cross ditches and water bars as staked or otherwise marked on the ground by Forest Service. When bridges and culverts are removed, associated fills shall also be removed to the extent necessary to permit normal maximum flow of water.

12. <u>Protection of Cultural Resources</u> Location of known historic or prehistoric sites, buildings, objects, and properties related to American history, architecture, archaeology and culture, such as settler or Indian artifacts, protected by American Antiquities Act of 1906 (16 U.S.C. 431-433), National Historic Preservation Act of 1966 (16 U.S.C. 470) and the Archaeological Resources Protection Act of 1979 (PL 96-95 and 36 CFR 261.9(e)) shall be identified on the ground by Forest Service. Forest Service may unilaterally modify or cancel this contract to protect an area, object of antiquity, artifact, or similar object which is or may be entitled to protection under these Acts regardless of when the area, object or artifact is discovered or identified. Discovery of such areas or objects by either party shall be promptly reported to the other party.

B-MS shall protect <> all known and identified historic or prehistoric sites, buildings, objects and properties related to American history, architecture, archaeology and culture against destruction, obliteration, removal or damage during B-MS's operations. In accordance with 36 CFR 296.14(c), B-MS shall bear costs of restoration, provided that such payment shall not relieve B-MS from civil or criminal remedies otherwise provided by law.

Wheeled or track-laying equipment shall not be operated within such areas except on roads, landings, tractor roads or skid trails approved under SP12. Unless agreed otherwise, trees will not be felled into such areas. B-MS may be required to backblade skidtrails and other ground disturbed by B-MS's operations within such areas in lieu of cross ditching required under SP10.

13. <u>Use of Timber</u> - This permit is subject to the Forest Resources Conservation and Shortage Relief Act of 1990 (101 Stat. 714-726; 16 U.S.C. 620 et. seq.).

Except for species determined pursuant to public hearing to be surplus, unprocessed Pacific yew meeting the minimum specifications identified in Clause 14 below shall not be exported from the United States nor used in direct or indirect substitution for unprocessed timber exported from private lands by B-MS or any person as defined in Section 493 (16 U.S.C. 620e) of the Act.

Timber in the following form will be considered unprocessed: (a) trees or portions of trees or other roundwood not processed to standards and specifications suitable for end product use; (b) lumber, construction timbers or cants, intended for remanufacturing, not meeting standards defined in Section 493 (16 U.S.C 620e) of the Act; and (c) Aspen or other pulpwood bolts exceeding 100 inches in length.

Unless otherwise agreed in writing, unprocessed Included Timber shall be delivered to a domestic processing facility and shall not be mixed with logs intended for export.

Prior to transfer, during the life of this permit, and for a period of 6 years from Termination Date, B-MS shall furnish to Forest Service upon request records showing the volume and geographic origin of unprocessed timber from private lands exported, or sold for export, by B-MS or affiliates.

Prior to delivering unprocessed Included Timber to another party, B-MS shall require each buyer, exchangee, or recipient to execute an acceptable agreement, which shall: (1) identify the federal origin of the timber, (2) specify domestic processing for the timber involved, (3) require the execution of such agreements between the parties to any subsequent transactions involving said timber, (4) require that all hammer brands and/or yellow paint must remain on logs until they are either legally exported or domestically processed, whichever is applicable, and (5) otherwise comply with the requirements of Section 492 (16 U.S.C. 620d) of the Act.

No later than 10 days following the execution of any such agreement between B-MS and another party, B-MS shall furnish to Forest Service a copy of each such agreement. B-MS shall retain, for 6 years from Termination Date, the records of all sales, exchanges, or dispositions of all Included Timber.

For breach of this provision, Forest Service may terminate this permit and take such other action as may be provided by statute or regulation, including the imposition of penalties. When terminated by Forest Service under this provision Forest Service will not be liable for any claim submitted by B-MS relating to the termination.

14. <u>Product Identification</u> - Unless Forest Service determines that circumstances warrant a written waiver or adjustment, (1) all Pacific yew logs that meet minimum standards of six (6) inches D.I.B. and 8 feet in length shall be hammer branded on both ends with an assigned brand, (2) all domestic

processing products shall be painted on both ends with highway yellow paint. B-MS will furnish and apply highway yellow paint of a lasting quality (oil base or equivalent). Paint sticks are not acceptable. Each paint mark must cover an area equal to a 2-inch circle.

All log or trees shall be branded with the assigned permit brand before removal from permit area. Such brands shall be State registered brands. Painting domestic processing products shall be done before removal from permit area.

All hammer brands and/or yellow paint must remain on logs until they are domestically processed. B-MS may remanufacture such products into different log lengths subject to agreement with Forest Service on surveillance by Forest Service. Remanufactured products to be removed from the area of remanufacture to another facility must be rebranded with the assigned sale brand unless otherwise agreed to in writing by Forest Service. For such remanufactured products, Forest Service may approve use of a State registered brand to be used exclusively as a catch brand, in lieu of the assigned sale brand. B-MS shall pay all surveillance costs except that Forest Service may waive such payment if such costs are minor and part of normal surveillance activities.

FIRE PROTECTION AND SUPPRESSION

15. B-MS shall bear the cost of suppressing fires on permit area caused by B-MS's operations: provided, that for each fire caused without negligence, B-MS's maximum liability for suppression costs is $300,000.00. For a fire caused or permitted to spread due to negligence or fault of B-MS's operations, including but not limited to smoking, warming fires , or failure to comply with the fire precautions and requirements herein; B-MS shall be responsible for the total cost of suppression and damages.

[Items 16 thru 25 are Standard Form R6-FS-6300-50 (5/89) Provisions]

16. Fire Period and Closed Season - Specific fire prevention measures are listed below and shall be effective for the period April 1 to October 31 of each year. The Forest Service may change the dates of said period by advance written notice if justified by unusual weather or other conditions. Required tools and equipment shall be kept currently in serviceable condition and immediately available for initial attack on fires.

17. Fire Plan - Before starting any operations on the project, B-MS shall prepare a fire plan in cooperation with the Authorized Officer providing for the prevention and control of fires in the project area.

The permittee shall certify compliance with fire protection and suppression requirements before beginning operations during the fire period and closed season, and shall update such certification when operations or equipment change.

18. Substitute Measures - The Authorized Officer may by written notice authorize substitute measures or equipment or may waive specific requirements during periods of low fire danger.

19. Emergency Measures - The Forest Service may require emergency measures, including the necessary shutting down of equipment or portions of operations in the project area during periods of fire emergency created by hazardous climatic conditions.

20. Fire Control - B-MS shall, independently and in cooperation with the Forest Service, take all reasonable action to prevent and suppress fires in the project area. Independent initial action shall be prompt and shall include the use of all personnel and equipment available in the project area.

For the purpose of fighting forest fires on or in the vicinity of the project, which are not caused by B-MS's operations, B-MS shall place employees and equipment temporarily at the disposal of the Forest Service. Any individual hired by the Forest Service will be employed in accordance with the Interagency Pay Plan for Emergency Firefighters. The Forest Service will compensate B-MS

for equipment rented, at fire fighting equipment rates common in the area or at prior agreed rates.

21. Compliance with State Forest Laws - Listing of specific fire precautionary measures herein is not intended to relieve B-MS in any way from compliance with the State Fire Laws covering fire prevention and suppression equipment, applicable to operations under this contract, permit or license.

22. Fire Precautions - Specific fire precautionary measures are as follows:

a. Smoking and Open Fires

Smoking and fires shall be permitted only at the option of B-MS. B-MS shall not allow open fires on the project area without advance permission in writing from Forest Service.

Unless restricted by State Law or Federal Regulation, smoking shall be permitted only in such portions of the project area that are free of flammable material. Smokers shall sit down to smoke in such a position that any burning material will fall within a cleared area, and shall extinguish and press out in mineral soil all burning material before leaving the cleared area.

b. Fire Extinguishers and Equipment, on Trucks, Tractors, etc.

All power-driven equipment operated by B-MS on National Forest land, except portable fire pumps, shall be equipped with one fire extinguisher having a UL rating of at least 5 B,C and one "D" handled or long handled round point shovel, size "O" or larger. In addition, each motor patrol, truck and passenger-carrying vehicle shall be equipped with a double-bit axe or Pulaski, 3-1/2 pounds or larger.

Equipment shall be kept in a serviceable condition and shall be readily available.

c. Power Saws

Each gasoline power saw operator shall be equipped with a pressurized chemical fire extinguisher of not less than 8-ounce capacity by weight, and one long handled round point shovel, size "O" or larger. The extinguisher shall be kept in possession of the saw operator at all times. The shovel shall be accessible to the operator within 1 minute.

d. Extinguishers

One refill for each type or one extra extinguisher sufficient to replace each size extinguisher required on equipment shall be safely stored in the fire tool box or other agreed upon place on the project area that is protected and readily available.

e. Spark Arresters and Mufflers

Each internal combustion engine shall be equipped with a spark arrester qualified and rated under USDA Forest Service Standard 5100-1a unless it is:

(1) Equipped with a turbine-driven exhaust supercharger such as the turbocharger. There shall be no exhaust bypass.

(2) A multi-position engine, such as on power saws which must meet the performance levels set forth in the Society of Automotive Engineers (SAE) "multi-positioned small engine exhaust fire ignition standard, SAE recommended practice J335B" as now or hereafter amended.

(3) A passenger carrying vehicle or light truck, or medium truck up to 40,000 GVW, used on roads and equipped with a factory designed muffler complete with baffles and an exhaust system in good working condition.

(4) A heavy duty truck, such as a dump or log truck, or other vehicle used for commercial hauling, used only on roads and equipped with a factory designed muffler and with a vertical stack exhaust system extending above the cab.

Exhaust equipment described in this Subsection, including spark arresters and mufflers, shall be properly installed and constantly maintained in serviceable condition.

f. Emergency Fire Precautions

B-MS shall restrict operations in accordance with the Industrial Fire Precaution Levels listed below. The Forest Service may change the Industrial Fire Precaution Levels to other values upon revision of the National Fire Danger Rating System and may change the specific Industrial Fire Precaution Levels when such changes are necessary for the protection of the National Forest. When sent to B-MS, the revised Industrial Fire Precaution Levels will supersede the attached levels.

INDUSTRIAL FIRE PRECAUTIONS SCHEDULE

LEVEL	INDUSTRIAL FIRE PRECAUTION
I.	Closed Season - Fire precaution requirements are in effect. A Fire Watch/Fire Security is required at this and all higher levels unless otherwise waived.
II.	Partial Hootowl - The following may operate only between the hours of 8 P.M. and 1 P.M. local time: a. power saws, except at loading sites b. cable yarding

c. blasting
d. welding or cutting of metal

III. Partial shutdown - The following shall be prohibited:

cable yarding - except that gravity operated logging systems employing non-motorized carriages may be operated between the hours of 8 P.M. and 1 P.M. local time when all blocks and moving lines are ten feet or more above the ground, excluding the line between the carriage and the choker.

power saws - except at loading sites and on tractor/skidder operations between the hours of 8 P.M. and 1 P.M. local time.

In addition, the following are permitted between the hours of 8 P.M. and 1 P.M. local time:

a. tractor/skidder operations
b. mechanized loading and hauling
c. blasting
d. welding or cutting of metal
e. any other spark-emitting operation not specifically mentioned

IV. General shutdown - All operations are prohibited.

The following definitions shall apply to these Industrial Fire Precaution Levels:

-Cable yarding systems: A yarding system employing cables and winches in a fixed position.

-Closed Season (Fire Precautionary Period): That season of the year when a fire hazard exists and as described in (1) the fire period and closed season.

-Hauling: Where hauling involves transit through more than one shutdown zone/regulated use area, the precaution level at the project area shall govern the level of haul restrictions, unless prohibited by other than the Industrial Fire Precaution Level system.

-Loading sites/woods site/project area: A place where any product or material (including but not limited to logs, firewood, slash, soil, rock, poles, posts, etc.) is placed in or upon a truck or other vehicle.

-Authorized Officer: The person executing the contract, permit or license on behalf of the Government and includes that persons designated representative, acting within the limits of their authority, or the duly appointed successor to the individuals.

-Tractor/Skidder Operations: A harvesting operation, or portion of a harvesting operation where tractors, skidders, or other harvesting equipment capable of constructing fireline, are actively yarding forest products and can quickly reach and effectively attack a fire

start.

Advance written waiver of the above precautions may be issued by the Authorized Officer.

Such waiver, or substitute precautions will prescribe measures to be taken by B-MS to reduce the risk of ignition, and/or the spread of fire. The Contracting Officer shall consider site specific weather factors, fuel conditions, and specific operations that result in less risk of fire ignition and/or spread than contemplated when precaution level was predicted. Consideration shall also be given to measures that reduce the precaution levels above. B-MS shall assure that all conditions of such waivers or substitute precautions are met.

B-MS shall obtain the predicted Industrial Fire Precaution Level daily, prior to the start of work, from the appropriate Ranger District headquarters. If predictions made after 6:00 P.M., local time, are significantly different than the original prediction, the Forest Service will inform B-MS when changes in restrictions or industrial precautions are made.

ATTACHMENT 3 PAGE 11

23. Fire Tools - B-MS shall furnish serviceable fire fighting tools in a readily accessible fire tool box or compartment of sound construction with a hinged lid and hasp so arranged that the box can be secured or sealed. The box shall be red and marked "Fire Tools" in letters at least one-inch high. It shall contain a minimum of:

(a) 2 axes or Pulaskis with a 32 inch handle.

(b) 3 adze eye hoes. One Pulaski may be substituted for one adze eye hoe.

(c) 3 long handled, round point shovels, size "0" or larger.

24. Fire Security - When the Industrial Fire Precautions Level is "I" or higher, unless a waiver is granted, B-MS shall designate a person who shall perform fire security services listed below on the project area and vicinity. The designated person shall be capable of operating B-MS's communications and fire fighting equipment specified in the contract, excluding helicopters, and of directing the activities of B-MS's personnel on forest fires. In lieu of having the designated person perform the required supervisory duties, B-MS may provide another person meeting the qualifications stated above to direct the activities of Contractor's personnel and equipment during all fire fighting activities.

Services described shall be for at least 1 hour from the time B-MS's Operations are shut down. For the purposes of this provision, personnel servicing equipment, and their vehicles, who are not engaged in cutting or welding metal are excluded.

Fire security services shall consist of moving throughout the operation area or areas constantly looking, reporting and taking suppression action on any fires detected. Where possible, the designated person shall observe inaccessible

portions of helicopter operating areas from vantage points within or adjacent to project area.

25. Blasting - Whenever the Industrial Fire Precaution Level is "II" or greater, a fire security person equipped with a long handled round point No. 0 or larger shovel and a five gallon backpack pump can filled with water, will stay at location of blast for one hour after blasting is done. Blasting may be suspended by Forest Service in writing, in an area of high rate of spread and resistance to control.

Fuses shall not be used for blasting. Explosive cords shall not be used without written permission of Forest Service, which may specify conditions under which such explosives may be used, and precautions to be taken.

SPECIAL PROVISIONS
TO ADMINISTRATIVE USE PERMITS
TO BE APPLIED WHEN APPROPRIATE AS DETERMINED BY B-MS'S OPERATION
OUTLINED IN EACH TRANSFER PERMIT

S1. Slash Disposal - B-MS shall deck all unutilized material, over <> inches d.i.b. at the large end and over <> feet long, at the landing or other approved location. All other slash greater than <> inch d.i.b. at the large end and over <> feet long shall be piled for later burning by Forest Service. Locations of piles shall not be within 20 feet of any live tree, unless otherwise agreed to in writing by Forest Service, or placed in streams, on roads, in ditches or other improvements.

As used in this contract the term slash is all vegetative material, including cull logs, blasted or pushed out stumps, chunks, broken tops, limbs, branches, rotten wood, damaged brush, damaged or destroyed reproduction, saplings or poles which is created by B-MS's operations under a permit including construction of roads or other improvements. Existing debris will be considered slash under this contract, where the disposal of such debris is necessary to adequately treat sale-generated slash, or where necessary to adequately provide for regeneration of the area cut over under this contract. Any burning of slash or refuse by B-MS can be done only after first obtaining a written permit from Forest Service and complying with its terms.

(((Specifications based on Forest by Forest Inputs)))

S2. Erosion Control - B-MS shall (1) avoid operating equipment when soil conditions are such that excessive damage will result; (2) construct erosion control structures as needed to control erosion; (3) repair promptly any existing erosion control structures damaged by B-MS operations; (4) complete seasonal erosion control work prior to suspending operations, and (5) perform other soil erosion control work as may be required under this permit.

Prior to suspension of operations or seasonal periods of precipitation runoff, B-MS shall remove ruts from roads and construct cross ditches, water bars, water-spreading ditches on landings, roads, and skid trails where staked or otherwise marked on the ground by Forest Service.

Where soil has been disturbed or displaced by B-MS's operations and measures described above will not result in satisfactory erosion control, and/or soil or site protection, the following revegetative work shall be performed where staked or otherwise marked on the ground by Forest Service:

a. Seed areas evenly with <> pounds per acre of a live pure seed mixture approved for such use by Forest Service. Seeding shall be done during the period <> to <>.

b. Fertilize seeded areas no later than 10 days

2 following seeding with <> pounds per acre of <> (standard commercial) fertilizer.

<u>(((Specifications based on Forest by Forest Inputs)))</u>

ATTACHMENT 4 PAGE 2

S3. <u>Tank Truck</u> - B-MS shall provide a tank truck or trailer, containing not less than 300 gallons of water, during yarding, loading, land clearing, right-of-way clearing and mechanical treatment of slash. A tank truck or trailer will not be required if powersaw falling and bucking is the only operation. Such tank truck or trailer shall be maintained in a serviceable condition and located within 10 minutes, round trip, from each project area during fire period and closed season.

The tank truck or trailer shall be equipped with a pump capable of discharging 20 gallons of water per minute, using a 1/4 inch nozzle tip, through a 50 foot length of rubber lined hose. In addition, 500 feet of serviceable fabric jacket rubber lined hose of not less than 1 inch outside diameter, fitted with a nozzle capable of discharging a straight stream of 1/4 inch diameter and a spray pattern shall be immediately available for use. The tank, pump and at least 250 feet of hose and nozzle shall be connected and ready for use at all times.

If a trailer is used, it shall be equipped with a hitch to facilitate prompt movement. A serviceable tow vehicle shall be immediately available for attachment to the trailer and must meet the time requirements stated above. Such truck or trailer shall be equipped to operate for a minimum of 8 hours. Tank truck or trailer shall be available from the start of work to the end of the Fire Watch/Fire Security service. [R6-FS-6300-53 (5/89)]

S4. <u>Communications</u> - B-MS shall provide adequate two-way communication facilities to report a fire to Forest Service within 15 minutes of detection. FCC Regulations prohibit commercial use of Citizen Band(CB) radios. (CB's are not considered adequate two-way communications).

Such communications shall be operable during periods of operation of power-driven equipment, including the time fire security is required. [R6-FS-6300-54 (5/89)]

Utilization Standards for Harvest of Pacific Yew Bark

The utilization of Pacific yew bark has two prameters: 1) the minimum size of material to be peeled, and 2) an established minimum amount of bark to be stripped from the trees in an area designated for peeling.

1) Unless otherwise provided for in a yew harvest prescription that designates certain yew to be left, yew bark should be harvested from pieces and stems which have a large end or top-of-stump diameter of at least 3 inches. On such pieces, the bark should be removed to a 1-inch small end diameter at the top of the stem and branches.

2) The goal is to collect all of the yew bark feasible to collect in designated areas. Realistically, on-the-ground, a collection of 95 percent is a practical goal. The other 5 percent could include bark in flutes, some trees that are unpeelable due to seized bark caused by damage or other factors, and an occasional tree that may not be found.

There are instances where a few trees are located in difficult to reach areas or far away from general collection area. Decisions as to whether or not this bark would be collected will be made by the local District Coordinators on a case-by-case basis.

Bristol-Myers Squibb Company
Pharmaceutical Group
Business Development and Planning
P.O. Box 4000 Princeton, NJ 08543-4000
609 252-5498 Fax: 609 252-6805

Zola P. Horovitz, Ph.D.
Vice President

April 29, 1992

Mr. D. Dean Bibles
State Director
Oregon and Washington State Office
Bureau of Land Management
1300 NE 44th Ave.
Attn. O.R. 910
Portland, OR 97208

Dear Mr. Bibles:

Enclosed are signed copies by Bristol-Myers Squibb of the 1991-92 Annual Pacific Yew Program Plan. We look forward to a continued productive relationship with the Bureau. Please return one signed copy to us.

Sincerely,

Zola P. Horovitz

Zola P. Horovitz

ANNUAL PACIFIC YEW PROGRAM PLAN

Bureau of Land Management

Oregon and Washington State Office

Fiscal Years 1991 and 1992

ANNUAL PACIFIC YEW PROGRAM PLAN
Bureau of Land Management
Oregon and Washington State Office
Fiscal Years 1991 and 1992

Table of Contents

ANNUAL PACIFIC YEW PROGRAM PLAN
Bureau of Land Management
Oregon and Washington State Office
Fiscal Years 1991 and 1992

I. INTRODUCTION

The goal of this FY 1991-92 Annual Pacific Yew Program Plan (1991-92 Plan) is to implement a Cooperative Agreement between Bristol-Myers Squibb (B-MS) and the Department of Interior/Bureau of Land Management (BLM). B-MS has entered into a similar Cooperative Agreement with the Department of Agriculture/Forest Service (Forest Service).

These Cooperative Agreements serve two principal purposes. First, they are part of a comprehensive federal strategy outlined in a Memorandum of Understanding (MOU) between the Department of Agriculture, the Department of Health and Human Services, and the Department of the Interior. This MOU expresses the commitment of these agencies to using their best efforts to ensure that adequate quantities of Pacific yew are available from the National Forests and other public lands to support the expeditious research and development of taxol. Taxol is a promising anticancer agent that is being developed pursuant to a Cooperative Research and Development Agreement (CRADA) between B-MS and the National Cancer Institute (NCI).

Second, the Cooperative Agreements reflect a commitment to maintaining the long-term viability of the Pacific yew as a structural component in forest ecosystems throughout its current range. Pursuant to the Agreements, the BLM and the Forest Service will create a comprehensive research program to study the ecology, silviculture and management of the species.

This 1991-92 Plan will provide details about the administration of the Cooperative Agreement between B-MS and the BLM, the inventory to be conducted pursuant to this Plan, the Pacific yew transfer process, programmatic NEPA compliance, the parties' harvesting goals, and funding requirements through September 30, 1992, which is the end of fiscal year 1992.

II. Definitions

A. PACIFIC YEW -- The Cooperative Agreement defines Pacific yew to include all portions of Taxus brevifolia including, but not limited to, bark, twigs, needles and other foliage. It is agreed that Pacific yew is broadly defined to maintain maximum authority on the part of BLM officers in designating Pacific yew for

transfer. BLM officers are under no mandate to transfer the entire Pacific yew tree to B-MS.

B. <u>DESIGNATED AGENT</u> -- An agent hired by B-MS to perform the functions necessary to harvest or collect Pacific yew offered for transfer to B-MS by the BLM. At this time, Hauser Chemical Research, Inc., and its subsidiary Hauser Northwest, Inc., (Hauser) will act as a Designated Agent of B-MS. B-MS may change its Designated Agent(s) or authorize other entities to act as Designated Agents upon written notification to the BLM. A Designated Agent is responsible for monitoring yew bark harvesting, including the establishment and maintenance of an automated data base containing specific details of each harvest document.

C. <u>DESIGNATED AGENT'S REPRESENTATIVE</u> -- A representative named in writing by a Designated Agent who has delegated authority to receive notices of harvestable yew and to sign Pacific yew harvest contracts. Designated Agent's Representatives are responsible for coordinating the activities of the Harvesters to accomplish yew harvest contract requirements in a timely and efficient manner.

D. <u>HARVESTER</u> -- Peelers, loggers, gleaners and other persons under the control and supervision of a Designated Agent or a Designated Agent's Representative who are authorized to collect or harvest Pacific yew for a Designated Agent.

E. <u>CONTRACTING OFFICER</u> -- A BLM Resource Area official having authority to execute Pacific yew harvest contracts and who can delegate authority to take action in connection with such contracts.

F. <u>AUTHORIZED OFFICER</u> -- A BLM Resource Area employee to whom has been delegated authority to take action in connection with Pacific yew harvest contracts.

G. <u>DESIGNATED BLM REPRESENTATIVE</u> -- A BLM Resource Area employee to whom has been delegated authority to administer Pacific yew harvest contracts.

H. <u>PUBLIC LANDS</u> -- All public lands under the administration of the Bureau of Land Management in Oregon and Washington.

I. <u>GROSS QUANTITY</u> -- The weight of yew bark prior to the drying process. Where bark is not peeled in the field, gross quantity will be measured by the total number of logs removed from a harvesting site.

J. CERTIFIED WEIGHT -- The weight of yew bark measured by the Designated Agent's Representatives on certified scales for the purpose of making payments to harvesters.

K. DISTRICT RANGER -- A uniformed BLM law enforcement officer stationed at each BLM district office.

L. BLM OR/WA PACIFIC YEW COORDINATOR -- An official of the BLM Oregon and Washington State Office to whom has been delegated the authority to attend meetings and take action on matters relating to the Annual Pacific Yew Program Plans and the Cooperative Agreement.

III. Administration

A. In General

1. To the extent practicable, the BLM, the Forest Service and B-MS will coordinate the activities, programs, and projects undertaken pursuant to the Cooperative Agreements and Annual Pacific Yew Program Plans.

2. All activities undertaken pursuant to the Cooperative Agreements and the Annual Pacific Yew Program Plans will be consistent with the MOU between the Department of Agriculture, the Department of Health and Human Services, and the Department of the Interior.

3. This 1991-92 Plan does not obligate BLM to sell any Pacific yew from public lands currently enjoined by court order.

4. B-MS will not use the 1991-92 Plan or any contract or transaction executed hereunder in such a manner so as to state or imply that the BLM endorses a product, project, or commercial line of endeavor.

5. B-MS will not use the 1991-92 Plan or the purposes hereunder to advertise its products, services, or purposes. B-MS will submit to the BLM for approval prior to distribution all press releases referring to the 1991-92 Plan, the BLM or the Department of the Interior, or the title of any employee thereof.

6. Nothing in the 1991-92 Plan shall be construed as obligating the BLM to expend, contract, or otherwise commit the United States to future

payment of funds in excess of appropriations authorized by law.

7. No member of, delegate to, or resident Commissioner in Congress shall be admitted to any share or part of the 1991-92 Plan, or any benefit that may arise therefrom, but this provision shall not be construed to extend to the 1991-92 Plan if made with a corporation for its general benefit.

8. Either party may terminate the 1991-92 Plan by providing written notice at least 30 days prior to the date of intended termination.

9. Consistent with the MOU and the Cooperative Agreements, B-MS will use Pacific yew obtained under the 1991-92 Plan to produce taxol in accordance with its obligations under the NCI taxol CRADA.

B. Meetings

1. Appropriate representatives from the Forest Service, the BLM, and B-MS will meet on an annual basis to discuss and agree on common elements of Annual Plans. Throughout the term of the Cooperative Agreements, annual meetings will be held on mutually agreeable dates.

2. Quarterly meetings will be held during the first month of each quarter of the fiscal year on a mutually agreeable date. At these quarterly meetings, or as otherwise appropriate, the representatives of the aforementioned parties will review implementation of the Cooperative Agreements and Annual Pacific Yew Program Plans, discuss and resolve problems arising thereunder, and generally coordinate Yew Program activities. The quarterly meetings will begin during the second quarter of fiscal year 1992. These meetings may be conducted via telephone conference call if agreed upon by the parties.

3. Thirty days prior to the quarterly and annual meeting dates, the Forest Service Region 6 Yew Coordinator will notify the representatives listed below of pertinent details, including the date, time, and place of the meetings. The 30-day notice requirement may be waived with respect to a particular meeting by mutual consent of the parties.

4. For FY 1991-92, BLM appoints the following representative to meet at the quarterly and annual meetings: Kent Tresidder, BLM OR/WA Pacific Yew Coordinator; Oregon State Office, Bureau of Land Management; P.O. Box 2965; Portland, Oregon 97208. Mr. Tresidder may, from time to time, designate other persons to accompany him to quarterly meetings, or to act in his stead as the official representative of BLM.

5. For FY 1991-92, B-MS appoints the following representative to meet at the quarterly and annual meetings: M. Dianne DeFuria; Senior Director, Business Development & Planning; Bristol-Myers Squibb Co., Pharmaceutical Group; P.O. Box 4000; Princeton, N.J. 08540. Ms. DeFuria may, from time to time, designate other persons to accompany her to meetings, and/or to act as an official representative of B-MS.

6. For FY 1991-92, the Forest Service appoints the following representatives or their designated substitutes to meet at the quarterly and annual meetings:

Washington Office Coordinator
Richard Miller

Region 1 Coordinator
Merrill Davis

Region 5 Coordinator
Mike Srago

Region 6 Coordinator
Fred Page

Pacific Northwest Station Coordinator
Pete Owston

National Forest at-large Representative
Jack Schlotter, Rogue River N.F.

7. Additional meetings may be held as needed, particularly during the harvesting season, to implement the Cooperative Agreements and the Annual Plans. If the topics to be discussed at these additional meetings are specific to either the Forest Service or the BLM, then the other agency may choose not to participate in the meetings.

C. Records

1. The BLM will keep such records as are required for the agency's approval and administration of the Cooperative Agreement, Annual Pacific Yew Program Plans, and all projects initiated thereunder.

2. Any request for copies of documents other than those approved for release by Cooperator, including the Cooperative Agreement, the Annual Pacific Yew Program Plans, or other related documents, must be in writing and comply with the Freedom of Information Act, 5 U.S.C. § 552 (FOIA).

3. B-MS shall submit to the BLM copies of redacted versions of the Cooperative Agreement, Annual Pacific Yew Program Plans, and other related documents that it considers appropriate for release to the public. These redacted versions will omit information that B-MS considers to be confidential commercial or financial information. If BLM personnel decide to release documents other than these redacted versions, then the agency must notify B-MS of its intent to release the information prior to its actual distribution. See Executive Order 12,600, 52 Fed. Reg. 23,781 (June 23, 1987) (See Attachment 1).

IV. Program Elements

A. Pacific Yew Inventory

1. In FY 1992, the BLM will take the steps necessary to initiate a comprehensive inventory of existing Pacific yew located on public lands in western Oregon.

2. Pursuant to a similar Cooperative Agreement between B-MS and the Forest Service, the Forest Service will conduct a comprehensive inventory of existing Pacific yew located on portions of six National Forests along the west slopes of the Cascade Mountain Range in Washington and Oregon, and a National Forest within the South Fork Clearwater River drainage in Idaho. To the extent practicable, the Forest Service and the BLM will coordinate their efforts, data, and analyses regarding these Pacific yew inventories.

3. The initial step in conducting the public lands Pacific yew inventory will be the identification of conditions where Pacific yew probably will

occur. The BLM will utilize all available data to stratify public lands for the probable locations of Pacific yew. The strata will be determined by an interdisciplinary team of district and State Office specialists. Maps delineating optimum, potential and other locations (strata) of Pacific yew will be produced for each of the areas to be surveyed in the public lands Pacific yew inventory.

4. Using these predictive maps, the Oregon State Office biometrician and forest inventory specialist will develop a recommended sampling design which will include the procedures used to select the timber areas to be sampled on the ground. Sampling design will be reviewed by outside sampling experts.

5. A detailed quantitative inventory of vegetative conditions will be made in the areas identified. Under the technical supervision of the State Office and district forest inventory specialists, BLM inventory plots will be measured in selected areas in accordance with standard vegetative sampling and measurement procedures modified to ensure adequate sampling of Pacific yew and associated habitat characteristics.

6. The vegetative plot data will be compiled and analyzed to determine size, quantity and distribution of Pacific yew. Field information will provide a vegetative data base for analyzing the Pacific yew occurrence in relation to other significant species and habitat characteristics.

7. BLM personnel engaged in other routine field inventories, including stand examinations, botanical inventories, wildlife surveys, and timber cruises, will be consulted for all relevant data on the occurrence and attributes of observed Pacific yew. This data will be used by BLM yew coordinators and forest inventory specialists responsible for conducting the public lands Pacific yew inventory. Relevant data will include written observations and aerial photography of plot location.

8. BLM personnel administering the public lands Pacific yew inventory will incorporate, to the extent practicable, all existing Pacific yew data.

9. To the extent possible, the determination of public lands to be sampled based on the stratification of Pacific yew occurrence will be completed by the end of April, 1992. Data collection by ground surveys will be initiated in the FY 1992 field season. It is anticipated that summarized Pacific yew inventory data and corresponding estimates of reliability will be available by August 31, 1992. To expedite the processing and analysis of inventory data, BLM will purchase computer hardware in the amount of $17,000 and software in the amount of $3,000. BLM will retain ownership of the computer hardware and software upon termination of the Cooperative Agreement. Thereafter, the BLM will analyze the inventory data and publish its public lands Pacific yew inventory findings as expeditiously as possible.

10. The BLM will provide the Forest Service Pacific Yew Environmental Impact Statement team with interim and final data from its public lands Pacific yew inventory as expeditiously as possible.

B. <u>Conservation Biology Guidelines</u>

1. BLM and Forest Service scientists and professionals will coordinate the development of interim Pacific Yew Conservation Biology Guidelines (Guidelines) based on available data and professional knowledge specific to the Pacific yew. The Guidelines will assure the viability of the Pacific yew in a tree form within stands and within its natural range. In promulgating these interim Guidelines, the BLM and the Forest Service will conduct, to the extent practicable, retrospective field examinations of the species' reactions to both natural and human-caused disturbances. The development of these interim Guidelines will include a thorough peer review. Target date for completion of the interim Guidelines is March 18, 1992. These Guidelines will serve on an interim basis for Pacific yew management until both a programmatic EIS and record of decision are completed.

2. Before promulgating revised Guidelines in later fiscal years, the BLM and the Forest Service will consider and incorporate findings from the Forest Service's conservation biology and confirmation

studies, and seek public comments on appropriate measures to include in the revised Guidelines.

C. Pacific Yew Research

1. The BLM and B-MS acknowledge the importance of a scientific foundation on which to base Pacific yew management decisions in order to sustain the long-term viability of the species. Pursuant to its Cooperative Agreement with the Forest Service, B-MS is funding an extensive Pacific yew research program that will study such issues as yew reproduction, yew growth and mortality, stand development, yew population and structure, and the vegetative, soil and animal components of pertinent forest ecosystems.

2. In FY 1992, BLM researchers may develop a Pacific yew research proposal after consulting and coordinating with Forest Service and Pacific Northwest Research Station scientists who are conducting Pacific yew research. The BLM proposal will include the purpose and method of study of the proposed research, manpower and equipment needs, funding requirements, and estimated time-line to completion. B-MS will review the completed research proposal and decide whether to provide funds in addition to the amounts specified in Schedule 1 to support a BLM Pacific yew research effort in FY 1992.

D. Pacific Yew Sales

1. Administration

a. The BLM will provide the necessary personnel and administrative services to direct the sale of Pacific yew located on public lands to B-MS as agreed to in the Cooperative Agreement and the 1991-92 Plan.

b. B-MS will name its Designated Agents in writing to the BLM. The Designated Agents will specify in writing to the BLM the names, addresses, business locations, and level of authority of individuals acting as Designated Agent's Representatives and Harvesters. Notification will be provided to the BLM OR/WA Pacific Yew Coordinator and will be sent within one week of designation of parties acting as Designated Agents,

Designated Agent's Representatives, and Harvesters.

c. Pacific yew will be sold by the BLM to B-MS in accordance with 30 U.S.C. §601, and 43 C.F.R. Subpart 5402. The BLM will sell Pacific yew to B-MS pursuant to a Vegetative or Mineral Material Negotiated Cash Sale Contract, Form 5450-5 (Attachment 2), or a Contract for the Sale of Vegetative Resources, Form 5450-1 (Attachment 3). Provisions covering environmental and administrative requirements for each sale will be attached to each contract.

d. B-MS, through its Designated Agents, will establish procedures requiring its Designated Agent's Representatives and Harvesters to comply with all terms and conditions of yew harvest contracts and interim and final Pacific Yew Conservation Biology Guidelines, when completed.

e. B-MS, through its Designated Agents, will establish procedures requiring its Designated Agent's Representatives and Harvesters to possess copies of appropriate documentation whenever they are harvesting and transporting Pacific yew from public and adjacent lands.

f. B-MS, through its Designated Agents, will establish procedures requiring its Designated Agent's Representatives and Harvesters to comply with all applicable environmental protection standards, contract stipulations and sale administrative procedures as enunciated by the BLM.

g. B-MS, through its Designated Agents and Designated Agent's Representatives, will provide a list of currently authorized Harvesters to each BLM District Ranger (Attachment 4) each Monday afternoon.

h. In the event that BLM personnel become aware of problems or violations of terms of the harvest contracts by the Designated Agent's Representatives and Harvesters, BLM representatives will immediately notify these parties of the problems or violations and any appropriate corrective action to be taken.

If problems or violations persist or are not rectified in a satisfactory manner or time period, BLM personnel may suspend operations under the applicable contract. Thereafter, the BLM must notify the appropriate Designated Agent of the problem or violation and the response to date.

If problems or violations are not satisfactorily resolved after notification of the appropriate Designated Agent, then the BLM must provide written notification to B-MS through the following individual (or her designated acting representative, supervisor or successor):

M. Dianne DeFuria
Senior Director
Business Development & Planning
Bristol-Myers Squibb Co.
Pharmaceutical Group
P.O. Box 4000
Princeton, N.J. 08540

If satisfactory corrective actions are not taken, or if the violation is serious, then the contract under which the problem or violation has occurred may be canceled by the BLM. The BLM may withhold new notices and contracts from the responsible Designated Agent's Representative until performance is completed to the satisfaction of the Contracting Officer or Authorized Officer. In the event that the BLM incurs expenditures to rectify or resolve damages as a result of breach of contract stipulations by B-MS's agents, then B-MS will reimburse the BLM for its reasonable and necessary direct expenditures, provided that B-MS has received written notice from the BLM about the causative problem or violation.

2. Identification of Pacific Yew Available for Sale

a. In FY 1991-92, the BLM will attempt to meet Pacific yew harvesting goals by evaluating existing sold and awarded timber sale contracts that are not currently enjoined in the following order:

i. Areas containing yew which was severed within the past 18 months where yew

harvest is required prior to prescribed burning;

ii. Approved and unapproved harvest units <u>prior</u> to felling of other species; and

iii. Areas where yew was previously harvested but which require yew reharvest to meet BLM yew utilization standards.

b. In all future timber sale contracts sold as part of the BLM's annual timber sale program, the BLM will retain ownership of Pacific yew under the terms of the contract. To the extent practicable, prelogging of Pacific yew will occur in harvest units of existing and future timber sale contracts.

3. <u>Notification of Pacific Yew for Harvest</u>

a. The BLM will provide B-MS's Designated Agents with written notice of every timber sale tract containing harvestable yew for B-MS pursuant to the Cooperative Agreement and Annual Pacific Yew Program Plans. When immediate action is warranted, the BLM Contracting Officer may provide the required notice by telephone to B-MS's Designated Agents.

b. In general, B-MS's Designated Agents will have 30 days to respond to a notice of harvestable yew by the BLM. However, the parties recognize that the need for immediate action occasionally may require a shorter response period. In those instances, the BLM will outline the nature of the immediate need and the deadline for a response date in its notice of harvestable yew.

c. B-MS, through its Designated Agents, will respond to every notice of harvestable yew by the BLM in a timely manner. The BLM may refuse to offer further contracts to Harvesters or Designated Agent's Representatives who willfully or consistently fail to respond to notices of harvestable yew in a timely manner. Additionally, the BLM may sell the Pacific yew covered by the notice to parties or entities other than B-MS.

d. Following a positive response of a Designated Agent, BLM officials will issue Pacific yew

harvest contracts in the following manner: "B-MS, acting through _______, its Designated Agent . . ."

e. To maximize yew recovery and minimize efforts, BLM and B-MS, through its Designated Agents, will evaluate those timber sale tracts having marginal quantities of harvestable yew to determine the most expeditious means of recovering the resource.

4. <u>Compliance with NEPA, FLPMA and other Applicable Statutes, Regulations and Policies</u>

a. The BLM will prepare all documents necessary to ensure that transfer of Pacific yew to B-MS pursuant to the Cooperative Agreement and Annual Pacific Yew Program Plans complies with applicable statutes, regulations, and policies. As appropriate, Pacific yew harvests will comply with all environmental laws and the state laws governing the transport of forest products.

b. To the extent possible, in FY 1991-92, BLM officials will sell to B-MS Pacific yew located in areas with existing NEPA documents which address the environmental impact of yew harvesting. Conforming amendments or corrections referencing yew harvesting will be made where necessary and allowable under NEPA.

E. <u>Programmatic Environmental Impact Statement</u>

1. A programmatic Environmental Impact Statement (EIS) will be prepared assessing the environmental consequences of various Pacific yew harvesting alternatives. The EIS will be prepared by a team of Forest Service specialists. The BLM and the Food & Drug Administration will be cooperating agencies in the EIS.

2. Recognizing the need to prepare this programmatic EIS as expeditiously as possible, the Forest Service has initiated work on the document before final data from the Pacific Yew Inventories are available. Forest Service and BLM personnel responsible for conducting the inventories will coordinate with the EIS team by providing interim and final inventory data for inclusion in the EIS as expeditiously as possible. The programmatic

EIS will be amended as necessary based on results from the inventories and the Conservation Biology studies. To the extent practicable, the EIS will address issues of interest to other agencies, including the BLM and the Food & Drug Administration.

3. Consistent with the critical nature of the programmatic EIS, on September 30, 1991, the Forest Service published in the Federal Register a Notice of Intent announcing the decision to prepare a programmatic EIS. The Forest Service will undertake those activities necessary to complete the EIS, including scoping, preparation of a draft EIS, solicitation and consideration of public comments, and preparation and publication of a final EIS.

4. Until the EIS is finalized, BLM actions taken pursuant to the Cooperative Agreement and Annual Pacific Yew Program Plans will be supported by appropriate NEPA documentation.

F. Accounting for Pacific Yew

1. B-MS, through its Designated Agents, will accept Pacific yew only when accompanied by documentation granting permission to harvest. B-MS, through its Designated Agents, will keep records of all Pacific yew transactions. B-MS, through its Designated Agents, will provide authorized BLM officials with necessary information from these records for use in determining the appraised value of Pacific yew which it sells to B-MS. Records will include the following information:

   a) date of transaction;
   b) name and address of person delivering Pacific yew;
   c) vehicle license number;
   d) land owner's name and address;
   e) legal description of harvest site and, as applicable, the contract number;
   f) quantity of Pacific yew delivered; and
   g) proof of authorization to harvest, as established in a contract or other document granting such permission.

2. B-MS, through its Designated Agents, will cooperate fully with the BLM in conducting law enforcement investigations pertaining to Pacific yew. Such cooperation shall include granting

access to harvest records necessary for the conduct of law enforcement investigations.

3. B-MS, through its Designated Agents, will maintain records of yew acquired under the Cooperative Agreement. Records will include the following information about each transfer:

a) BLM District;
b) Resource Area;
c) Contract Number;
d) Timber Sale Name;
e) Legal Description;
f) Pacific Yew Trip Ticket Numbers;
g) Unit of Measure (lbs. of bark; no. of logs if bark is not peeled on site);
h) Gross Quantity;
i) Date of Transaction;
j) Name of Designated Agent's Representative;
k) Name and Address of Harvester; and
l) Vehicle License Number of Harvester.

4. B-MS, through its Designated Agents and Designated Agent's Representatives, will check the gross quantity of yew appearing on each Pacific Yew Trip Ticket against the certified quantity measured by the Designated Agent's Representative for payment to the harvester. The Designated Agent's Representative will enter the certified weight on each ticket and then promptly mail the tickets, first class postage prepaid, to the BLM. Discrepancies of more than 10% will be reported immediately by the Designated Agent's Representative to the respective District Ranger (Attachment 4). BLM will purchase approximately 50 scales, worth a total of $1500, to accomplish gross weight measurements of Pacific yew bark by Designated BLM Representatives in the field. BLM will retain ownership of these scales upon termination of the Cooperative Agreement.

5. B-MS's Designated Agents will provide the BLM with summaries by contract number and by Harvester of Pacific yew collected under BLM contracts. The two-week summaries will be forwarded to the BLM OR/WA Pacific Yew Coordinator on Thursday afternoons following the close of each two-week period.

6. B-MS's Designated Agents will also provide a monthly accounting which will include the information in paragraph 3, above. The monthly

accounting will be forwarded to the BLM OR/WA Pacific Yew Coordinator within 15 days of the end of the preceding month.

V. Harvesting Goals

A. <u>In General</u>

1. The FY 1992 goal for yew harvesting by B-MS pursuant to the Cooperative Agreements and Annual Pacific Yew Program Plans is at least 750,000 pounds of dried bark from Pacific yew located on lands under the control of either the Forest Service or the BLM.

2. The FY 1992 goal for yew harvesting by B-MS pursuant to the Cooperative Agreements and Annual Pacific Yew Program Plans is approximately 40,000 gross pounds of bark from Pacific yew located on public lands under the control of the BLM.

3. Under the terms of the Cooperative Agreement and 1991-92 Plan between B-MS and the BLM, the BLM agrees to make available areas, as defined in these documents, for the collection of Pacific yew in accordance with all applicable laws, regulations, and policies to meet the FY 1992 harvesting goals for Pacific yew located on public lands.

B. <u>Limits on Pacific Yew Harvesting by Third Parties</u>

1. The BLM and B-MS recognize the need to ensure that legitimate research efforts by parties other than B-MS to produce taxol for use in humans be allowed to proceed. On the other hand, the realities of current taxol sourcing, and the government-wide commitment to cooperating with the NCI's CRADA partner, dictate that reasonable limits be placed on third parties' harvesting of Pacific yew located on federal lands.

2. The FY 1992 limit for transfer, by sale or otherwise, of Pacific yew located on the public lands to parties other than B-MS is 1,000 gross pounds of Pacific yew bark per research project, and 5,000 gross pounds of Pacific yew bark overall, for use in the research or development of taxol for use in humans.

3. Until further notice from B-MS, there is no limit on the amount of Pacific yew needles or other

foliage that can be transferred, by sale or otherwise, from the public lands to parties other than B-MS for use in the research or development of taxol for use in humans. Until further notice from B-MS, the BLM may sell debarked Pacific yew logs to any party irrespective of its participation in taxol research and development. The parties acknowledge that B-MS may amend this policy during the term of the 1991-92 Annual Plan.

4. The parties agree that if B-MS cannot practicably utilize all portions of Pacific yew trees sold by the BLM for purposes consistent with the NCI CRADA, then the BLM may sell these portions of Pacific yew trees to other parties. Yew sold to other parties under these circumstances is not subject to the conditions described in Paragraphs 2 and 3, above.

VI. Funding

A. <u>Funding Levels</u>

1. In FY 1991 and FY 1992, B-MS will provide the BLM with adequate funds to support the programs and activities outlined in the Cooperative Agreement and the 1991-92 Plan. Without B-MS's prior written approval, this amount will not exceed the funding level identified in Schedule A of the Cooperative Agreement. The parties acknowledge that the sum in Schedule A is an estimate which could be subject to change depending on circumstances beyond the control of either party, including bids received to conduct the inventory, court orders, and legal challenges.

2. Recognizing that implementation of the Yew Program has required the BLM to incur substantial start-up costs during FY 1991 and the first two quarters of FY 1992, B-MS will make an initial deposit in accordance with Schedule 1 to the Pacific Yew Account within 15 days of execution of the FY 1991-92 Plan. Additional deposits will be remitted by B-MS in advance and on a quarterly basis to cover FY 1992 costs in accordance with Schedule 1.

3. To the extent possible, the funds in the Pacific Yew Account will be allocated in a manner consistent with a document entitled "Pacific Yew Program Needs Estimate; Fiscal 1991-1992" and attached hereto as Schedule 1.

4. It may become apparent to BLM personnel that the Pacific Yew Account does not contain sufficient funds to complete the agency's obligations for FY 1991 and FY 1992, as outlined in the Cooperative Agreement and the 1991-92 Plan. In this event, the BLM will provide B-MS with its estimate of the additional funds needed, and a description of the activities to be completed with these funds. B-MS will have the sole right to decide whether to remit additional sums to the BLM to support the specified activities. The BLM and B-MS will mutually agree upon how to allocate the remaining funds among the FY 1991-92 Program Elements if B-MS elects not to remit additional funds to the Pacific Yew Account.

B. Accounting Procedures

1. The BLM will establish a special account, to be known as the Pacific Yew Account, in its Oregon/Washington (OR/WA) State office. B-MS will remit the funds called for under the Cooperative Agreement and the 1991-92 Plan to the Pacific Yew Account. To the extent possible, the OR/WA State Office will distribute these funds according to Schedule 1 of the 1991-92 Plan.

2. The BLM will provide B-MS with an estimate of yew program expenses twenty days prior to the beginning of each quarter.

3. Initially, BLM will provide B-MS with a quarterly accounting statement twenty-five days after the end of each quarter; these quarterly statements will present a current balance for the Pacific Yew Account and itemized deposits to and expenditures from the Account. Thereafter, following implementation of the Federal Financial System within BLM by the end of 1992, these accounting statements will include a breakdown of the costs associated with each Program Element, a brief description of the services or goods purchased with the money, an entry for indirect or overhead costs, the total expenditures for the quarter, and other information as agreed upon by the BLM and B-MS. Additionally, the BLM will provide B-MS with documents verifying the itemized expenditures from the Pacific Yew Account.

4-29-92
Date

Zola Horovitz, Ph.D.
Vice President, Business
Development and Planning
Bristol-Myers Squibb Company

5/1/92
Date

D. Dean Bibles
State Director, Oregon and
Washington State Office
Bureau of Land Management

Presidential Documents

Executive Order 12600 of June 23, 1987

Predisclosure Notification Procedures for Confidential Commercial Information

By the authority vested in me as President by the Constitution and statutes of the United States of America, and in order to provide predisclosure notification procedures under the Freedom of Information Act concerning confidential commercial information, and to make existing agency notification provisions more uniform, it is hereby ordered as follows:

Section 1. The head of each Executive department and agency subject to the Freedom of Information Act shall, to the extent permitted by law, establish procedures to notify submitters of records containing confidential commercial information as described in section 3 of this Order, when those records are requested under the Freedom of Information Act (FOIA), 5 U.S.C. 552, as amended, if after reviewing the request, the responsive records, and any appeal by the requester, the department or agency determines that it may be required to disclose the records. Such notice requires that an agency use good-faith efforts to advise submitters of confidential commercial information of the procedures established under this Order. Further, where notification of a voluminous number of submitters is required, such notification may be accomplished by posting or publishing the notice in a place reasonably calculated to accomplish notification.

Sec. 2. For purposes of this Order, the following definitions apply:

(a) "Confidential commercial information" means records provided to the government by a submitter that arguably contain material exempt from release under Exemption 4 of the Freedom of Information Act, 5 U.S.C. 552(b)(4), because disclosure could reasonably be expected to cause substantial competitive harm.

(b) "Submitter" means any person or entity who provides confidential commercial information to the government. The term "submitter" includes, but is not limited to, corporations, state governments, and foreign governments.

Sec. 3. (a) For confidential commercial information submitted prior to January 1, 1988, the head of each Executive department or agency shall, to the extent permitted by law, provide a submitter with notice pursuant to section 1 whenever:

(i) the records are less than 10 years old and the information has been designated by the submitter as confidential commercial information; or

(ii) the department or agency has reason to believe that disclosure of the information could reasonably be expected to cause substantial competitive harm.

(b) For confidential commercial information submitted on or after January 1, 1988, the head of each Executive department or agency shall, to the extent permitted by law, establish procedures to permit submitters of confidential commercial information to designate, at the time the information is submitted to the Federal government or a reasonable time thereafter, any information the disclosure of which the submitter claims could reasonably be expected to cause substantial competitive harm. Such agency procedures may provide for the expiration, after a specified period of time or changes in circumstances, of designations of competitive harm made by submitters. Additionally, such

procedures may permit the agency to designate specific classes of information that will be treated by the agency as if the information had been so designated by the submitter. The head of each Executive department or agency shall, to the extent permitted by law, provide the submitter notice in accordance with section 1 of this Order whenever the department or agency determines that it may be required to disclose records:

(i) designated pursuant to this subsection; or

(ii) the disclosure of which the department or agency has reason to believe could reasonably be expected to cause substantial competitive harm.

Sec. 4. When notification is made pursuant to section 1, each agency's procedures shall, to the extent permitted by law, afford the submitter a reasonable period of time in which the submitter or its designee may object to the disclosure of any specified portion of the information and to state all grounds upon which disclosure is opposed.

Sec. 5. Each agency shall give careful consideration to all such specified grounds for nondisclosure prior to making an administrative determination of the issue. In all instances when the agency determines to disclose the requested records, its procedures shall provide that the agency give the submitter a written statement briefly explaining why the submitter's objections are not sustained. Such statement shall, to the extent permitted by law, be provided a reasonable number of days prior to a specified disclosure date.

Sec. 6. Whenever a FOIA requester brings suit seeking to compel disclosure of confidential commercial information, each agency's procedures shall require that the submitter be promptly notified.

Sec. 7. The designation and notification procedures required by this Order shall be established by regulations, after notice and public comment. If similar procedures or regulations already exist, they should be reviewed for conformity and revised where necessary. Existing procedures or regulations need not be modified if they are in compliance with this Order.

Sec. 8. The notice requirements of this Order need not be followed if:

(a) The agency determines that the information should not be disclosed;

(b) The information has been published or has been officially made available to the public;

(c) Disclosure of the information is required by law (other than 5 U.S.C. 552);

(d) The disclosure is required by an agency rule that (1) was adopted pursuant to notice and public comment, (2) specifies narrow classes of records submitted to the agency that are to be released under the Freedom of Information Act, and (3) provides in exceptional circumstances for notice when the submitter provides written justification, at the time the information is submitted or a reasonable time thereafter, that disclosure of the information could reasonably be expected to cause substantial competitive harm;

(e) The information requested is not designated by the submitter as exempt from disclosure in accordance with agency regulations promulgated pursuant to section 7, when the submitter had an opportunity to do so at the time of submission of the information or a reasonable time thereafter, unless the agency has substantial reason to believe that disclosure of the information would result in competitive harm; or

(f) The designation made by the submitter in accordance with agency regulations promulgated pursuant to section 7 appears obviously frivolous; except that, in such case, the agency must provide the submitter with written notice of any final administrative disclosure determination within a reasonable number of days prior to the specified disclosure date.

Sec. 9. Whenever an agency notifies a submitter that it may be required to disclose information pursuant to section 1 of this Order, the agency shall also notify the requester that notice and an opportunity to comment are being

provided the submitter. Whenever an agency notifies a submitter of a final decision pursuant to section 5 of this Order, the agency shall also notify the requester.

Sec. 10. This Order is intended only to improve the internal management of the Federal government, and is not intended to create any right or benefit, substantive or procedural, enforceable at law by a party against the United States, its agencies, its officers, or any person.

Ronald Reagan

THE WHITE HOUSE,
June 23, 1987.

[FR Doc. 87-14602
Filed 6-23-87; 4:38 pm]
Billing code 3195-01-M

Number	UNITED STATES DEPARTMENT OF THE INTERIOR BUREAU OF LAND MANAGEMENT
85120570	VEGETATIVE OR MINERAL MATERIAL NEGOTIATED CASH SALE CONTRACT *($999 or less)*

State

District

Date of Sale

Name of Purchaser *(first, middle, last)*

Address *(include zip code)*

KIND OF PRODUCT	EST. QTY. *(Units)*	RATE/ UNIT	PRICE
			$
		TOTAL	$

Purchaser is liable for total purchase price shown above. There will be no refunds. Additional payment, if any, will be made in accordance with Sec. 1(c). This contract is made under terms of Sec. 1( ) and the stipulations indicated.

Contract expires *(date)*	ALL MATERIALS MUST BE RE-MOVED PRIOR TO THIS DATE

Location of sale:

RECEIVED AS PAYMENT IN FULL

ACCOUNT	COUNTY	PRICE
P. D. (5881)		$
O & C (5882)		
CBWR (5897)		
Road Maintenance Fee (9110) or (9120)		
Material Site Reclamation (5310) or (5320)		

Purchaser certifies that he is twenty-one years of age or older and a citizen of the United States.

Signature of Purchaser

Signature of Authorized Officer

SEC. 1 CONTRACT TERMS
(check appropriate block)

☐ (a) All materials in contract area in excess of estimated quantity are reserved by the Government. ☐ Severence ☐ removal in excess of that quantity will subject Purchaser to trespass action.

☐ (b) The quantity of material is a predetermined amount and may be more or less than the actual amount.

☐ (c) If total number of units ☐ severed ☐ removed exceeds estimated units additional units shall be paid for at unit rate at time and place designated by the Authorized Officer.

SEC. 2 GENERAL STIPULATIONS
(check appropriate block)

All materials are to be removed in strict accordance with instructions of Authorized Officer and the following conditions and requirements:

No material may be ☐ severed ☐ removed unless marked or otherwise designated by Authorized Officer. Title to material sold under this contract shall remain in Government and shall not pass to Purchaser until such material has been removed from contract area. If this contract involves severence of vegetative material, risk of loss shall be borne by Purchaser after material is cut. Nothing herein shall be construed to relieve Purchaser from liability for any breach of contract or any wrongful or negligent act, or for any violation of any applicable regulation of the Department of the Interior.

Purchaser shall take such measures for prevention and suppression of fire on the contract area and other Government lands as are required by applicable laws and regulations. Purchaser shall dispose of refuse in accordance with instructions from Authorized Officer.

SEC. 3 SPECIAL STIPULATIONS

Form 5450-5 (November 1984)
(See instructions on reverse of District copy)

DISTRICT

Attachment 2

Form 5450–1
(June 1989)

UNITED STATES
DEPARTMENT OF THE INTERIOR
BUREAU OF LAND MANAGEMENT

CONTRACT FOR THE CASH SALE
OF VEGETATIVE RESOURCES

Issuing Office

Contract Number

THIS CONTRACT is made and entered into the day of , 19 , under the authority of Executive Order (L.U. Lands) or the Act of August 28, 1937 (50 Stat. 874) as amended, (43 U.S.C. Sec. 1181a–f), relating to the revested Oregon and California Railroad and reconveyed Coos Bay Wagon Road grant lands, or under the Act of July 31, 1947 (61 Stat. 681) as amended, (30 U.S.C. Secs. 601–604), relating to other lands under the jurisdiction of the Bureau of Land Management, and the regulations as set forth in 43 CFR Group 5400, between the UNITED STATES OF AMERICA, hereinafter called Government, acting through the Bureau of Land Management, and

of , hereinafter called Purchaser.

WITNESSETH, That the parties hereto do mutually agree as follows:

Sec. 1. *Vegetative Resources Sold.* Government hereby sells to Purchaser and Purchaser hereby buys from Government, under the terms and conditions of the contract, the vegetative resources listed in Sec. 2 within the area described below comprising the contract area and situated in the County of
State of , and described as follows:

TOWNSHIP	RANGE	SECTION	SUBDIVISION(S)

Sec. 2. *Total Purchase Price.* (a) Purchaser agrees to pay Government as the total purchase price for the vegetative resources sold hereunder, the sum of dollars ($).

KIND OF VEGETATIVE RESOURCE	QUANTITY *(Units Specified)*

All vegetative resources in the contract area in excess of the quantity listed above are reserved to Government.

(b) The total purchase price shall be paid in full on or before the date this contract is signed by the Authorized Officer. Payment hereunder shall be made by cash, money order, bank draft, or check made payable to the Bureau of Land Management.

Sec. 3 *Bond.* A performance bond shall be filed by Purchaser on or before the date the contract is signed by the Authorized Office in the sum of

($) which bond shall be forfeited to the amount of the damages determined by the Authorized Officer if all the provisions of this contract are not faithfully and fully performed by Purchaser. If the amount of the damages exceed the amount of the bond, Purchaser hereby agrees to pay the excess. Upon satisfactory performance of all provisions of this contract, the bond shall be cancelled, or if cash or negotiable securities are furnished in lieu of a surety bond, such cash or negotiable securities shall be returned to Purchaser.

Sec. 4. *Time for Extraction, Cutting, and Removal.* Purchaser may commence cutting, extraction, and removal of vegetative resources sold under this contract on the date this contract is signed by the Authorized Officer. Purchaser's right to cut, extract, and remove such vegetative resources shall expire ( ) months after such date; *Provided, however,* extension of time may be granted as provided in 43 CFR Subpart 5463 and 5473.

Sec. 5. *Standard and Special Provisions.* The rights and obligations of the parties hereto shall be subject to the Standard Provisions set forth in Secs. 6 through 16 and to any Special Provisions contained under Sec. 17 on the reverse hereof.

Attachment 3

PURCHASER, sign here	UNITED STATES OF AMERICA
(Name of Firm)	By (Name)
(Name)	(Title)
(Address)	(Date)

STANDARD PROVISIONS

Sec. 6. *Definitions Used in this Contract:*
(a) "Authorized Officer" means any employee of the Bureau of Land Management to whom has been delegated the authority to take action in connection with this contract.
(b) "Vegetative Resources" means all vegetative material which cannot be measured in units of board feet of timber.

Sec. 7. *Passage of Title and Risk of Loss.* Title to the vegetative resource sold under this contract remain in Government and shall not pass to Purchaser until such vegetative resources have been severed or extracted. Risk of loss shall be borne by the party holding title, *except* that nothing herein shall be construed to relieve either party from liability for any breach of contract or any wrongful or negligent act.

Sec. 8. *Violations, Suspension, and Cancellation.* If Purchaser violates any of the provisions of this contract, the Authorized Officer may, by written notice, suspend any further operations of Purchaser under this contract, *except* such operations as may be necessary to remedy any violations. If Purchaser fails to remedy all violations within thirty (30) days after receipt of the suspension notice, the Authorized Officer may, by written notice, cancel this contract and take appropriate action to recover all damages suffered by Government by reason of such violation.

Sec. 9. *Fire Prevention and Slash Disposal.* Purchaser shall take such measures for the prevention and suppression of fire on the contract area and other adjacent Government lands or other Government lands used or traversed by Purchaser in connection with operations under this contract as are required by applicable laws and regulations. However, when in the opinion of the Authorized Officer, weather and other conditions affecting fire incidence and control make special precautions necessary to protect the contract area and said Government lands, Purchaser shall take such additional or other fire prevention and control measures as may be required by the Authorized Officer. Disposal of slash shall be done in accordance with a plan approved by the Authorized Officer.

Sec. 10. *Trespass.* If in connection with operations under this contract Purchaser, his contractors, subcontractors, or the employees of any of them, cuts, injures, or removes any Government materials, other than the vegetative resources sold under this contract, Purchaser shall be liable for damages under applicable law. Purchaser shall pay Government for such damages after written demand therefor by the Authorized Officer.

Sec. 11. *Responsibility for Damage Suffered, Cost, or Expense Incurred by Government.* Purchaser shall be liable for any damage suffered, cost, or expense incurred by Government arising out of any operations under this contract whenever such damage, cost, or expense results from any breach of contract or wrongful or negligent act of Purchaser, his contractors, subcontractors, or the employees of any of them. Purchaser shall pay Government for such damage, cost, or expense after written demand therefor by the Authorized Officer.

Sec. 12. *Disclaimer of Warranty.* Government expressly disclaims any warranty of the fitness of the vegetative resources for any purpose of Purchaser; all vegetative resources sold hereunder are accepted "as is" without any warranty of merchantability by Government. Any warranty as to the quantity or quality of the vegetative resources sold hereunder is expressly disclaimed by Government.

Sec. 13. *Simultaneous Use of Contract Area by Others.* If the Authorized Officer determines that other use of the contract area will not seriously interfere with the operations of Purchaser, he may issue permits, leases, or contracts for the simultaneous use of the contract area by others.

Sec. 14. *Equal Opportunity* — The Purchaser will comply with all provisions of Executive Order No. 11246 of September 24, 1965, as amended, and of the rules, regulations, and relevant orders of the Secretary of Labor.

Sec. 15. *Officials Not to Benefit.* No Member of, or Delegate to, Congress, or Resident Commissioner, after his election or appointment, or either before or after he has qualified and during his continuance in office, and no officer, agent, or employee of the Department of the Interior, except as provided in 43 CFR 7.4(a)(1), shall be admitted to any share or part in this contract or derive any benefit that may arise therefrom; and the provisions of Sec. 3741 of the Revised Statutes of the United States, as amended (41 U.S.C. Sec. 22), and Secs. 431, 432, and 433, Title 18, U.S.C. relating to contracts, enter into and form a part of this contract so far as the same may be applicable.

Sec. 16. *Appeal.* An appeal may be taken from any decision of any officer of the Bureau of Land Management to the Board of Land Appeals pursuant to the Rules of Practice (43 CFR Part 4 Subpart E).

Sec. 17. *Special Provisions.* Purchaser shall comply with the following special provisions unless otherwise authorized, in writing, by the Authorized Officer:

Statement of

Dr. Bruce Chabner
Director
Division of Cancer Treatment
National Cancer Institute

Before the

Subcommittee on Fisheries and Wildlife
Conservation and the Environment
Committee on Merchant Marine and Fisheries

Subcommittee on National Parks and Public Lands
Committee on Interior and Insular Affairs

Subcommittee on Forests, Family Farms, and Energy
Committee on Agriculture

United States House of Representatives

Hearing on

H.R. 3836, The Pacific Yew Act of 1991

March 4, 1992

Mr. Chairman and members of the subcommittees, thank you for inviting me to testify before you today regarding the drug taxol. I am Dr. Bruce Chabner, Director of the Division of Cancer Treatment at the National Cancer Institute. I am accompanied today by Mr. Reid Adler, Director of the Office of Technology Transfer at the National Institutes of Health.

I am pleased to have the opportunity to bring you up to date on the development of this important anticancer agent.

We appreciate the active support the Congress has shown in expediting our efforts to increase the availability of taxol for cancer patients. The Pacific Yew Act of 1991 is an example of the high level of interest and support this effort has received from Congress; however, as its provisions do not bear directly on the programs and activities of the Department of Health and Human Services, we defer to our sister agencies to take a position on the bill.

Since many of the effective anticancer agents now in use are derived from natural products, we currently focus our discovery efforts on this vast and mostly untapped source of potentially very important agents.

We test extracts of natural products from plant and animal sources in screening systems that use panels of human tumor cell

lines and select active extracts for further testing, chemical characterization, and clinical development. Because the plant or animal sources for these compounds frequently may be in limited supply or even endangered because of expansion of urbanization and destruction of habitat, our steadfast policy has been to protect the interests and ecology of the countries and communities that provide samples for these efforts. One year ago, we sponsored an international conference to define measures that will protect and preserve biodiversity in the environment. The result of that meeting has been a joint effort by the National Science Foundation, the State Department, and the NCI to support an environmentally sound program to identify pharmaceuticals from plant and animal species in developing countries.

One of the most promising natural products to be discovered through the NCI screening and development process is taxol. Taxol was originally isolated in 1971 from the bark of _Taxus brevifolia_, although subsequently we have found that it is present in the bark and needles of a variety of taxus species. Although taxol showed minimal activity in initial preclinical testing, it was later demonstrated to have a unique biochemical mechanism of action and a high degree of activity in selected non-human test systems. At each step, significant problems of production, supply, formulation, and clinical toxicity hampered its development. In 1988 activity against ovarian cancer was first observed, and in subsequent trials the drug produced

response rates of about 30 percent in patients who had failed standard therapy, with some of these responses lasting more than one year.

Taxol has also demonstrated significant activity against breast cancer and is being tested for activity against several other types of cancer. This is a promising therapy for many thousands of cancer patients and its development is a very high priority for NCI. Unfortunately, as you know, the drug has been in critically short supply, but due to the combined efforts of NCI, Bristol-Myers Squibb, the Bureau of Land Management, and the Forest Service we have made significant progress.

Currently the only reliable source of taxol for use in patients is an extract from the bark of the Pacific Yew tree, a tree native to the old growth forests of the Pacific Northwest. The concentration of taxol in each tree is very small, and about three trees are required to produce sufficient amounts of taxol to treat a single patient.

The combined potential population of patients with breast and ovarian cancer who may be candidates for treatment with taxol is approximately 50,000 persons per year, a number far in excess of the 500 patients per year receiving the drug in clinical trials before the cooperative efforts began. This year we will be able to treat at least 8 - 10,000 patients with the available supply

of taxol produced from bark harvested in 1991. This is a direct result of the cooperation between several federal agencies and the private sector.

Our supplies are adequate to support several of our highest priority studies, but additional meritorious research could be initiated if the supplies were larger. It is impossible for me to predict what the supply situation will be at the time of drug approval, since this will depend on a number of factors beyond our control.

Since the passage of the Stevenson-Wydler Technology Innovation Act of 1980 and the Federal Technology Transfer Act of 1986, it is a national policy to transfer federally-owned or originated technology to the private sector whenever appropriate. The Act also encouraged, as a national policy, joint research and development projects between government laboratories and industry. Indeed, these are duties of each laboratory.

NCI has followed the policy of seeking partners in private industry to commercialize its discoveries and inventions. In order to assure the further development and eventual marketing of taxol, in 1990 NCI entered into a Cooperative Research and Development Agreement (CRADA) with a pharmaceutical company, Bristol-Myers Squibb (BMS).

The purpose of this CRADA is to expedite the development of taxol as an antitumor agent, and to generate data necessary to obtain FDA approval for this compound. The CRADA between NCI and BMS does not address the issue of compensation for utilization of yew trees. This matter has been addressed by the Forest Service and the Bureau of Land Management in their agreements with BMS.

The CRADA was awarded to BMS following a full and open competition, including publication in the Federal Register, and a thorough scientific review by government scientists of the four separate proposals submitted. Under the CRADA, BMS has undertaken the complicated and expensive production of taxol and has cooperated with NCI in performing the necessary clinical trials. To date, BMS has made impressive progress and has exceeded the goals set forth under the CRADA. In exchange, NCI has agreed to provide BMS with access to its clinical and preclinical data on an exclusive basis solely for use in obtaining approval for the commercial marketing of taxol. Further, NCI has reserved the right to publish the results of its studies with taxol.

Because the very first developmental work occurred and was published many years ago (indeed prior to the enactment of the Federal Technology Transfer Act), there currently is no government-owned patent protection for this agent. The CRADA, however, is an extremely useful mechanism through which to link

NCI's continuing laboratory and clinical research interests in taxol with BMS's product development efforts. Under the CRADA, NCI and BMS scientists have collaborated on the design, oversight and implementation of clinical trials required for FDA approval and on additional research and development of taxol. This collaboration has accelerated the pace of development of taxol and will allow its introduction into the standard arsenal of approved anticancer agents in the near future, assuming that taxol continues to be found safe and effective.

The NCI does not have the capacity to develop and market taxol as a prescription drug on its own, nor does any other government agency. Nor has NCI the legal authority to market drugs. While BMS has obtained orphan drug status from the FDA for taxol in ovarian cancer patients, other companies are free to pursue the development of taxol for other diseases. In addition, NCI, through its own research and development programs, is vigorously attempting to develop other taxol-like drugs. These would be available through patent licensing on a competitive basis to all pharmaceutical companies.

In recognition of the need to establish a fair and reasonable price for taxol, the text of the CRADA also includes an acknowledgement by BMS that in developing a fair market price for taxol, consideration will be given to the public investment in taxol research and development and the health and safety needs of

the public. This language is very similar to the fair pricing clause that is included in the model CRADA used by NIH and ADAMHA. A similar clause was present in our license agreement with BMS for the anti-AIDS drug ddI (Videx). In that instance, we believe that the company established a very favorable price for their product, below that of its major competitive product, AZT. Because taxol is not patented, other companies are able to develop this compound for use in treating breast and other types of cancer. Additionally, other companies are developing taxol analogues, some of which conceivably might be more effective or less toxic than taxol itself. It should be recognized that taxol's development will provide a "road map" for the development of taxane and other analogues. We believe that these market forces also will limit the price of taxol.

In order to assist BMS in obtaining Pacific Yew tree bark, NCI has worked with other Federal agencies with jurisdiction over Federal lands that have large concentrations of Pacific Yew trees. Those other agencies, the U.S. Department of Agriculture Forest Service and the Department of the Interior Bureau of Land Management, have entered into a Memorandum of Understanding (MOU) with NCI's parent agency, the Department of Health and Human Services. Under the terms of the MOU, all agencies are cooperating to provide Pacific Yew trees to BMS to meet the urgent requirements of drug supply for current research clinical trials.

In addition, the Departments of Interior and Agriculture have signed cooperative agreements with BMS to facilitate access to Pacific Yew tree bark from Federal lands. These understandings have been very effective in allowing large-scale collection of yew bark for taxol production over the past year.

Taxol production has increased significantly over the past year due to the excellent cooperation of all parties, and we now have approximately one and a half kilograms per month for clinical trials. This has enabled us to allow NCI Clinical and Comprehensive Cancer Centers to provide taxol for certain ovarian cancer patients through an NCI established Treatment Referral Center (TRC). The TRC refers patients who would qualify for this protocol or similar protocols to participating Cancer Centers. Over 800 patients have received taxol at these regional cancer centers in the first five months of this program.

The use of yew bark for this purpose has engendered much interest on the part of local businesses and environmentalists who are concerned about the economic and environmental impact of harvesting the Pacific Yew. In order to respond to these concerns, agency officials have met with representatives of various groups, both in Washington D.C. and in Portland, Oregon and in general have gained their support for the effort to direct all available supplies of Taxus bark to the clinical trials program. I call your attention to the fact that, as part of the

MOU, BMS has supported a government survey of yew trees on Federal lands, and the USDA has undertaken the establishment of a comprehensive plan for harvesting and protection of the yew.

While for the next one to two years we feel that the harvesting of Taxus bark will be the only effective source for this much needed drug, the long-term solution to the supply problem does not rest with harvesting Pacific Yew trees. The NCI and BMS are working with the biomedical and agricultural research communities to develop alternative methods to produce taxol. These include total synthetic production, partial synthesis, alternative renewable sources, such as needles or twigs, cultivation of faster-growing species, plant tissue culture, hydroponics, etc., all of which would eliminate the need for tree bark.

During the past year, significant progress has been made in these areas. NCI grantees have been able to synthesize the complex taxane ring that lies at the core of the taxol molecule. Other scientists have succeeded in synthesizing the full molecule on an experimental scale, starting with a precursor, Baccatine III, found in needles of the yew and in commercial taxol plants. Renewable sources of taxol have been identified in commercial nursery plants of the yew family, as well as in the needles of taxus trees in India, Australia and Europe. With NCI and USDA support, a consortium of commercial nurseries, led by the Zelenka Nursery of Michigan and the University of Mississippi, has

collected large amounts of yew needles from cultivated stock, and has found that this biomass contains substantial amounts of taxol. Because these cuttings are readily available, they constitute a potentially promising source of drug. I am confident that within two to three years we will no longer be dependent on the Pacific Yew as the sole source of this drug.

The NCI has also taken steps to encourage the rapid development and evaluation of new approaches to production of taxol and analogues to taxol. On an emergency basis, NCI provided supplemental funds to grantees conducting research in this area throughout the country to speed up this process.

In addition, on July 27, 1990, NCI issued a Request for Applications (RFA) asking that investigators in the biomedical research community submit new grant applications for Biological and Chemical Studies of Taxol. In response to the RFA, 61 proposals were received and 16 grants totaling $2.3 million were awarded last year. The NCI is also encouraging other private pharmaceutical companies to enter the search for active taxol-like compounds that do not require extraction from tree bark.

We have recently signed an agreement to aid in the testing of a taxol analogue, taxotere, under the sponsorship of a BMS competitor, Rhone-Poulanc, a French pharmaceutical company with subsidiaries in the United States. Taxotere appears to have

promising chemical activity in ovarian cancer, and the company holds several patents on this compound. We will join the company in testing taxotere as a single agent and in combination against ovarian cancer, lung cancer, and other common solid tumors. As this drug is manufactured from precursors found in yew needles, the company will not need to depend on the harvest of trees for its production.

We know that there is great commercial interest in taxol-related compounds and have encouraged this work with grant support, conferences, and staff contacts. We plan to hold an international conference on taxol and related compounds in the fall of 1992.

Perhaps a few words indicating the current limitations of taxol are in order. First, while taxol is an important new experimental drug, it is not a cure for cancer. This drug has certain side-effects that may make its use medically inappropriate in certain cases. Therefore, any decision about the use of this drug must be undertaken by highly qualified medical staff familiar with the side-effects and activity of the agent.

Second, taxol is still an experimental agent. It is not for sale. Its use is carefully regulated by the FDA and other applicable government agencies. Any use of the drug would need to conform to the applicable standards for experimental agents regulated by the FDA. Such use would require adherence to

principles of informed consent, suitability to enter a research protocol, etc. Not every patient is suitable to enter a taxol research protocol. The physicians at NCI are available to assist primary care physicians to determine the medical eligibility of patients for clinical trials using taxol as well as identifying other treatment options that may be more suitable, when taxol is not available or medically appropriate. Our treatment referral center advises physicians regarding appropriate alternatives for patients with ovarian cancer or breast cancer who have failed primary treatment.

In conclusion, I would like to emphasize that NCI recognizes the serious environmental and economic issues surrounding the development of taxol. We have worked carefully with other Federal agencies, the research community, and the private sector to formulate a responsible and environmentally sound policy to meet this public health need. Our first priority has been to ensure the most rapid testing and broadest availability of this agent, an effort that requires the cooperation of government, the public, and a commercial partner. As public officials, we recognize our responsibilities to the American people and to the Congress to ensure that our actions are in the best interest of the public health, but appropriately balanced with other priorities, such as protecting the environment.

We welcome the opportunity to appear before you today to address your concerns. I would be happy to answer any questions you may have.

We welcome the opportunity to appear before you today to address your concerns. I would be happy to answer any questions you may have.

Appendix F

Pacific Yew Inventories

Appendix F

Inventory

Introduction

Prior to 1991, the Forest Service had no inventory method specifically designed to measure the number of Pacific yew. Any available information was usually obtained as part of inventories designed to measure commercial timber values and volumes. Because Pacific yew is distributed in the forest differently from most commercial species (lower density and clumpy), an inventory design for yew must differ from one that measures relatively homogeneous species, such as Douglas-fir. The inventory providing the best available information of yew stocking (before 1991) was that performed by the Forest Inventory and Analysis Group (FIA) of the Pacific Northwest Research Station (PNW). FIA inventories are ongoing low-intensity, multi-species samples that include Pacific yew. However, the FIA inventories only sampled state and private lands and thus did not supply the kind of information needed for an environmental impact statement for federal lands. Most early estimations of the existing yew populations were developed from this FIA data.

In early 1991, when it became clear that better population information was needed, the Forest Service began developing inventory and procedures for Oregon and Washington. This inventory was field-tested in the summer of 1991, with the inventory completed in 1992. Concurrently, the Forest Service in Idaho and the Bureau of Land Management in Oregon developed similar but unique inventory procedures that were used during the 1992 field season. It is these inventories that are used in this document to estimate outputs from the alternatives.

In addition to the large-scale inventories that have been taken, site-specific surveys have been carried out by both agencies. These were used to determine where bark harvest could be implemented for the 1991 and 1992 harvest programs. These surveys concentrated on recently harvested timber sales and areas with approved environmental assessments. As more site-specific planning continues, more surveys will be needed to determine the exact locations of Pacific yew stands.

The following sections will describe the inventory and modeling procedures used by the Forest Service Pacific Northwest Region (Region Six), Forest Service Northern Region (Region One), and the BLM. Tables showing the results from the modeling include a combined table for each inventory (Region Six, Region One, and BLM), and a series of tables that separate the inventory by forest and BLM district. All three inventories have been combined into one series of tables and can be found in the Pacific yew population and inventory section of Chapter IV.

Forest Service, Pacific Northwest Region

The Region Six inventory provides information on the characteristics of the vegetation where yew is found. Such characteristics include overstory and understory tree species composition and size distribution; amount and type of existing regeneration; plant association; and distribution of standing dead trees. The implementation of this inventory began during the summer and fall of 1991. Plots measured during 1991 were used in a preliminary analysis to determine if additional sampling was needed. It was determined that more samples were indeed needed, and the inventory was completed during the 1992 field season. The following sections describe the development and methodology of this inventory and report the results.

Inventory Design

Due to the importance of developing quality inventory estimates as soon as possible at a reasonable cost, an inventory design that would minimize the number of field plots to be sampled was chosen. To accomplish this, either a prediction would need to be made as to where Pacific yew would occur and those acres more intensely inventoried, or the acres with a low probability of having yew would need to be eliminated from the inventory.

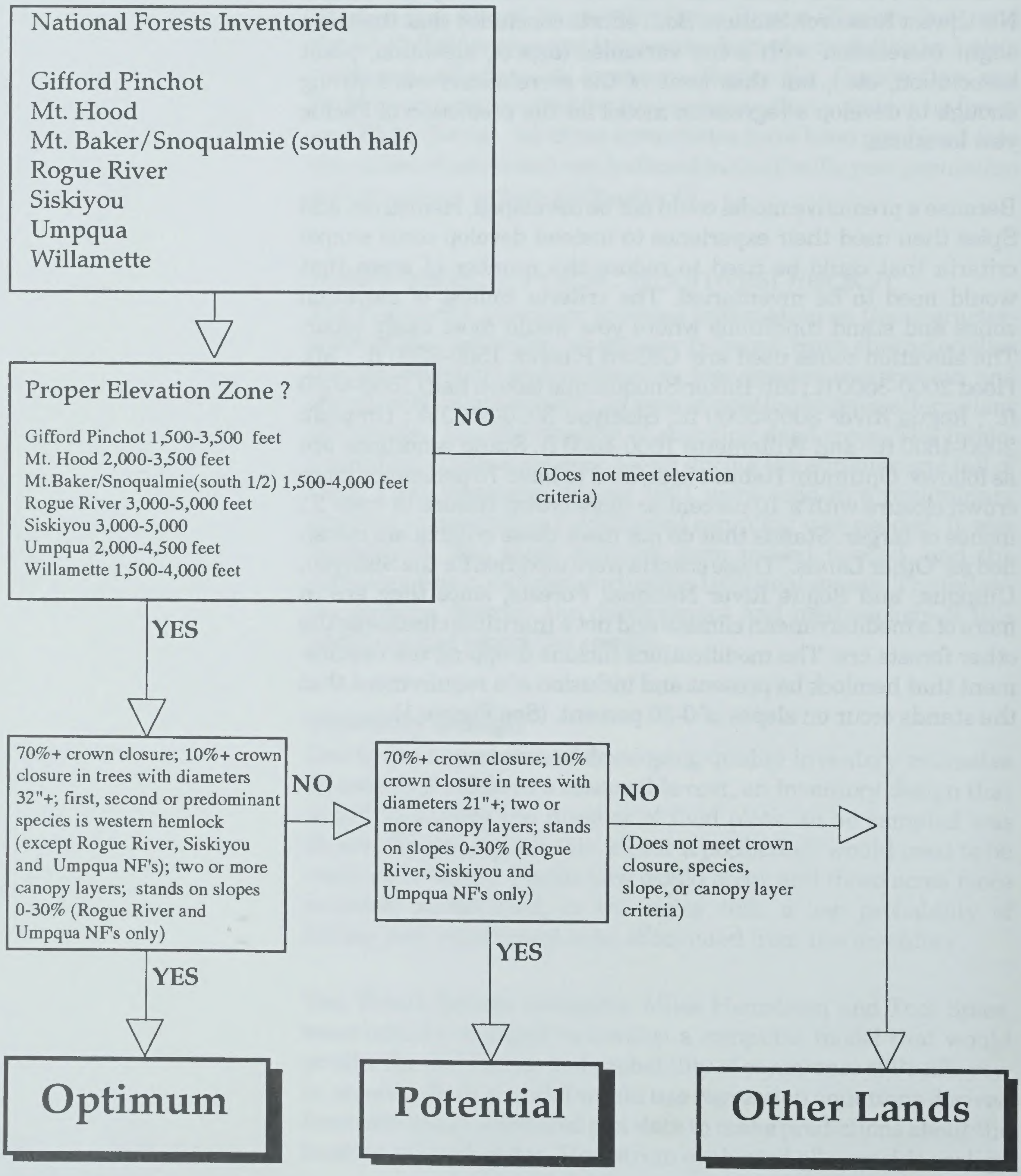
Two Forest Service ecologists, Miles Hemstrom and Tom Spies, were initially engaged to develop a computer model that would predict the abundance and probability of occurrence of Pacific yew in an area. Such a model would use regression equations derived from previously measured plot data to make predictions about the location of yew habitat. Hemstrom evaluated all westside ecology

data that had been collected on the six national forests, while Spies evaluated research data that had been collected by the Pacific Northwest Research Station. Both efforts concluded that there is a slight correlation with some variables (aspect, elevation, plant association, etc.), but that none of the correlations were strong enough to develop a regression model for the prediction of Pacific yew locations.

Because a predictive model could not be developed, Hemstrom and Spies then used their experience to instead develop some simple criteria that could be used to reduce the number of acres that would need to be inventoried. The criteria consist of elevation zones and stand conditions where yew would most likely occur. The elevation zones used are: Gifford Pinchot 1500-3500 ft. ; Mt. Hood 2000-3500 ft.; Mt. Baker/Snoqualmie (south half) 1500-4000 ft. ; Rogue River 3000-5000 ft.; Siskiyou 3000-5000 ft.; Umpqua 2000-4500 ft.; and Willamette 1500-4000 ft. Stand conditions are as follows: Optimum Habitat is defined to have 70 percent or more crown closure with a 10 percent or more crown closure in trees 21 inches or larger. Stands that do not meet these criteria are classified as "Other Lands." These criteria were modified for the Siskiyou, Umpqua, and Rogue River National Forests, since they are in more of a mediterranean climate and not a maritime climate as the other forests are. The modifications include dropping the requirement that hemlock be present and inclusion of a requirement that the stands occur on slopes of 0-30 percent. (See Figure 1).

Figure F-1

Criteria Used to Identify Potential Pacific Yew Habitat



Mapping of the three habitat types was done using data from a computerized satellite land information system (Landsat) in conjunction with a geographical information system (GIS). Resolution for the Landsat data was based on 25 X 25 meter pixels. In other words, each 25 x 25 square meter of the national forest was classified as either Optimum, Potential, or Other, based on the above criteria. A contractor (Pacific Meridian) was employed to produce this pixelized map of the forests which resided as a layer of data in the GIS computer. The contractor then divided the forests into five-acre cells each composed of approximately 32 pixels. The computer then tallied the number of pixels in each of the three habitat types within each of the five-acre cells. Each cell was then classified into one of 13 strata based on the mix of Potential, Optimum, and Other acres. (See Table F-1.)

This type of methodology has not previously been used by the Forest Service for forest inventory purposes. However, Landsat data recently gathered for information on old growth forests had the same characteristics needed for yew inventories.

Table F-1

Pacific Yew Inventory Strata

Stratum Number	Description of Strata
01	4 or more acres are potential; remaining acres can be optimum or other
02	4 or more acres are optimum; remaining acres can be potential or other
03	4 or more acres are other; remaining acres can be potential or optimum
04	3 to 3.9 acres are potential; remaining acres can be optimum or other
05	3 to 3.9 acres are optimum; remaining acres can be potential or other
06	3 to 3.9 acres are other; remaining acres can be potential or optimum
07	2 to 2.9 acres are potential; one or less acre is other; remaining acreage is optimum
08	2 to 2.9 acres are optimum; one or less acre is other; remaining acreage is potential
09	2 to 2.9 acres are potential; one or less acre is optimum; remaining acreage is other
10	2 to 2.9 acres are optimum; one or less acre is potential; remaining acreage is other
11	2 to 2.9 acres are other; one or less acre is potential; remaining acreage is optimum
12	2 to 2.9 acres are other; one or less acre is optimum; remaining acreage is potential
13	All other combinations

On each forest, 100 cells per stratum were randomly selected by computer to serve as a possible sampling population. The selected grid cells were printed on a mylar overlay of the forest's ortho quad map. The forest inventory coordinator eliminated cells that were not totally composed of lands managed by that particular forest. Thirty cells were then selected from those that remained and represented the maximum across all districts on the forest. Each grid cell was transferred from the forest's overlay map to 1:12,000 scale aerial photographs and then located in the field. At the end of the 1992 field season, 1875 plots had been sampled in the region.

During field implementation of the program, crews were sent out to the five-acre grid cells to record occurrences of the following:

- Number of Pacific yew trees
- All live trees meeting designated specifications (all species)
- Canopy layers
- Crown closure
- Vegetative indicator species
- Live yew regeneration
- Dead trees
- Down woody material
- Dead yew trees with symptoms of *Phytophthora lateralis* infection

Within each square five-acre grid cell, the crews systematically apportioned several areas for the various types of measurements required. First, three belt-transects one chain wide (66 feet) were installed to solely record the occurrence of Pacific yew. Second, four circular plots were installed. Each of these four plots consisted of three concentric plots: a variable radius plot, a 1/20 acre fixed radius plot, and a 1/100 acre fixed radius plot. Within the variable radius plot, all live trees with a 19" Diameter at Breast Height (DBH, 4.5 feet high) and greater were recorded using a 40 Basal Area Factor prism (a measuring device used to determine which trees would be sampled). Within the 1/20 acre fixed radius plot, live trees 5"-18.9" DBH, cover canopy layers, crown closure, forest vegetative indicator species, and groupings of hardwood trees were recorded. Within the 1/100 acre fixed radius plot, live regeneration from 6" tall to 4.9" DBH was recorded.

In addition, two belt-transects, one chain wide, were installed to record dead trees; and line transects were installed to record down woody material.

Lastly, dead Pacific yew 3" DBH or greater were recorded and examined to determine the presence of *Phytophthora lateralis*, a root disease associated with Port-Orford-cedar. Information on the presence and severity of root disease pockets within the cell were also recorded.

Modeling Process

The computer modeling of the Region Six data was done by a contractor Mason, Bruce and Girard, Inc., (MB&G). The Forest Service supplied yew inventory data, summarized into stand tables by DBH, for each of the 13 strata in its yew inventory. These data came from field inventories the Forest Service conducted in 1991 and 1992. These stand tables were obtained by summarizing only the plots on which Pacific yew was found. The Forest Service also supplied, by stratum, the total number of plots and the number of plots on which yew occurred so that the amount of yew available could be proportionally reduced.

The Forest Service also supplied the acres in each inventory strata and classified how those acres would be treated in the alternatives. The different classes reflected whether yew harvesting was allowed by the forest plan. Provisions were also made to exclude yew harvest in riparian zones in harvested areas.

The Forest Service data was supplied in spreadsheets. MB&G's first step was to convert the basic stand tables and tables of acres into a relational database (Microrim's R:Base). Data was then checked to ensure that all data supplied by the Forest Service was properly converted.

Bark weight calculations for each diameter class in the Forest Service stand tables were made using the Bureau of Land Management's relationships of stump diameter and height to pounds of bark. These calculations made the conservative assumption that stump diameter and DBH are the same. Trees between two and three inches in diameter were assumed to have two pounds of bark.

The alternatives designate levels of harvest in terms of the maximum percent of trees harvested and the minimum number of trees (for three diameter classes) left (see Chapter II). Quite simply, yew harvest can remove up to the maximum percent allowed (under the alternatives) so long as the required minimum number of trees are left.

The harvesting parameters set forth in the Description of Alternatives were fed into a program which produced a summary of harvestable yew trees and weight for each land class in each stratum and alternative.

Results

The following tables display the results of modeling the alternative using the inventory data from Region Six.

All National Forests - Region 6 (Oregon and Washington)							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	5,426,510	41,396,000	0	0	0	0	0
B	5,426,510	41,396,000	91,650	389,000	200-290	1,897,000	950-1,430
C	5,426,510	41,396,000	2,184,100	2,319,600	1,160-1,740	7,493,960	3,750-5,620
D	5,426,510	41,396,000	2,184,100	3,976,900	1,990-2,990	12,433,160	6,220-9,320
F	5,426,510	41,396,000	2,184,100	6,586,300	3,300-4,940	22,375,280	11,190-16,790
G1	5,426,510	41,396,000	2,184,100	4,953,300	2,480-3,710	23,716,840	11,860-17,790
G2	5,426,510	41,396,000	3,143,330	6,881,200	3,440-5,160	29,061,720	14,530-21,800

*Trees >1" DBH

Gifford Pinchot National Forest							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	982,560	8,955,300	0	0	0	0	0
B	982,560	8,955,300	14,840	60,200	30-45	122,360	61-92
C	982,560	8,955,300	324,880	371,800	186,279	710,400	355-533
D	982,560	8,955,300	324,880	679,400	190-285	1,288,240	644-966
F	982,560	8,955,300	324,880	995,100	498-746	1,886,440	943-1,415
G1	982,560	8,955,300	324,880	688,600	344-516	1,400,640	700-1,050
G2	982,560	8,955,300	560,210	1,153,200	577-865	2,276,720	1,138-1,708
*Trees >1" DBH							

Mt. Baker-Snoqualmie National Forest							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	533,710	6,797,400	0	0	0	0	0
B	533,710	6,797,400	1,510	11,300	6-8	34,960	17-26
C	533,710	6,797,400	90,580	174,100	87-131	485,120	243-364
D	533,710	6,797,400	90,580	336,800	168-253	935,040	468-701
F	533,710	6,797,400	90,580	499,700	250-375	1,385,440	693-1,039
G1	533,710	6,797,400	90,580	343,500	172-258	1,066,200	533-800
G2	533,710	6,797,400	163,260	616,700	308-463	1,820,280	910-1,365
*Trees >1" DBH							

Mt. Hood National Forest							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	609,560	1,961,300	0	0	0	0	0
B	609,560	1,961,300	7,750	12,700	6-10	47,160	24-35
C	609,560	1,961,300	293,740	115,800	58-87	354,080	177-266
D	609,560	1,961,300	293,740	203,500	102-153	614,280	307-461
F	609,560	1,961,300	293,740	335,000	168-251	986,600	493-740
G1	609,560	1,961,300	293,740	247,800	124-186	917,800	459-688
G2	609,560	1,961,300	364,550	317,100	159,238	1,241,160	621-931
*Trees >1" DBH							

Roque River National Forest							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	543,770	8,732,600	0	0	0	0	0
B	543,770	8,732,600	9,200	99,200	50-74	582,000	291-437
C	543,770	8,732,600	252,670	670,100	335-503	2,555,160	1,278-1,916
D	543,770	8,732,600	252,670	1,240,100	620-930	4,517,080	2,259-3,388
F	543,770	8,732,600	252,670	1,944,800	972-1,459	9,350,680	4,675-7,013
G1	543,770	8,732,600	252,670	1,411,700	706-1,059	8,278,840	4,139-6,209
G2	543,770	8,732,600	334,650	1,787,800	894-1,341	9,578,880	4,789-7,184
*Trees >1" DBH							

Siskiyou National Forest							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	477,540	352,800	0	0	0	0	0
B	477,540	352,800	8,350	5,600	3-4	51,680	26-39
C	477,540	352,800	128,770	10,200	5-8	66,240	33-50
D	477,540	352,800	128,770	11,100	6-8	69,320	35-52
F	477,540	352,800	128,770	29,400	15-22	147,800	74-111
G1	477,540	352,800	128,770	46,300	23-35	424,160	212-318
G2	477,540	352,800	128,770	46,400	23-35	424,360	212-318
*Trees >1" DBH							

Umpqua National Forest							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	916,810	6,083,200	0	0	0	0	0
B	916,810	6,083,200	25,690	115,200	58-86	633,240	317-475
C	916,810	6,083,200	449,740	478,100	239-359	1,662,240	831-1,247
D	916,810	6,083,200	449,740	783,900	392-588	2,503,040	1,252-1877
F	916,810	6,083,200	449,740	1,328,300	664-996	4,139,880	2,070-3,105
G1	916,810	6,083,200	449,740	1,065,900	533-799	5,860,040	2,930-4,395
G2	916,810	6,083,200	580,340	1,300,200	650-975	6,511,160	3,256-4,883
*Trees >1" DBH							

Willamette National Forest								
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	1,362,560	8,513,400	0	0	0	0	0
B	1,362,560	8,513,400	24,310	84,800	42-64	425,600	213-319
C	1,362,560	8,513,400	643,720	499,500	250-375	1,660,720	830-1,246
D	1,362,560	8,513,400	643,720	722,100	361-542	2,506,160	1,253-1,880
F	1,362,560	8,513,400	643,720	1,454,000	727-1,091	4,478,440	2,239-3,359
G1	1,362,560	8,513,400	643,720	1,149,500	575-862	5,769,160	2,885-4,327
G2	1,362,560	8,513,400	1,008,850	1,659,800	830-1,245	7,326,160	3,663-5,495

*Trees >1" DBH

Forest Service, Northern Region

Because Region One did not have any existing Landsat data or GIS information, a different inventory design was utilized. At the time of the Region One inventory, it was felt that the only area where yew was at high enough concentrations to be harvestable was on one portion of the Nez Perce National Forest. Although Pacific yew does occur in smaller concentrations in other places, it would take take a tremendous effort to sample and it is unlikely that additional areas suitable for harvest would be located. At the time of inventory, shrub-form Pacific yew on the Flathead National Forest was not considered a viable resource and was not included as part of the inventoried area. This is similar to what was done in Region Six when it was decided to concentrate inventory efforts on westside forests. Both efforts would produce conservative estimates of the total number of trees.

Inventory Design

An inventory area composed of 136,000 acres was located on the Nez Perce National Forest. The area was divided into a series of polygons using stand atlas and moose winter range maps. Based on expected yew density, moose winter range status, and accessibility, each polygon was classified into three sampling intensities:

None - (No Sample) yew expected infrequently or not at all;

Low - (0.5 Percent Sample) low density patches or scattered yew expected across polygon. (Areas with poor access); and

High - (1 Percent Sample) High density patches or continuous yew expected across polygon.

Crews located and measured 1/20th acre (26.3') fixed plots evenly spaced through the polygon that was sampled. Those polygons which were classified as low potential for having yew had plots spaced on a 10x10 chain (66-foot) grid. This produced a sampling intensity of .5 percent of the area. Polygons classified as high probability of yew had plots spaced on a 7x7 chain grid, thus producing a 1.0 percent sampling intensity. At each plot the following attributes were recorded:

--Yew crown closure;
--Crown closure of non-yew species;
--Primary and secondary overstory species;
--Occurrence of past logging;
--Moose use;

--Slope, aspect, and topography;
--Whether the plot was located in a riparian area;
--Presence or non-presence of certain browse species; and
--General tree information (diameter class, stem count, height).

Modeling Process

An Oracle database was used to process the plot information and to model the output from the alternatives. The approach was similar to what was done for Region Six, except this method did not allow for simulation of a minimum number of leave trees. Consequently, the results show little difference between alternatives which include the number of leave trees as a variable.

Results

The following table displays the results of modeling the alternatives using the inventory data from Region One.

Nez Perce National Forest (only Forest in Region 1)							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	136,312	6,944,000	0	0	0	0	0
B	136,312	6,944,000	3,070	78,000	40-60	454,000	230-340
C	136,312	6,944,000	67,870	1,199,000	600-900	3,819,000	1,910-2,870
D	136,312	6,944,000	67,870	1,615,000	810-1,220	6,277,000	3,140-4,710
F	136,312	6,944,000	67,870	2,033,000	1,020-1,520	8,736,000	4,370-6,560
G1	136,312	6,944,000	67,870	1,615,000	810-1,220	8,736,000	3,140-4,710
G2	136,312	6,944,000	67,870	1,615,000	810-1,220	8,736,000	3,140-4,710

*Trees >1" DBH

Bureau of Land Management

After reviewing the results from the Region Six, 1991 Pacific yew inventory, the BLM developed similar procedures for collecting information. Because the BLM did not have any existing Landsat data and only partial GIS stand coverage, the agency utilized more local knowledge in determining where to concentrate their inventories.

Inventory Design

All BLM forested areas, constituting slightly more than two million acres on six districts in western Oregon, were inventoried for Pacific yew. Each of the six districts were stratified into two-to-six strata based on the district's determination as to the probability of finding yew. The southern districts, where yew was known to occur in large quantities, were stratified to a greater extent than on northern districts, where yew was less likely to occur.

Strictly speaking, the inventory design consisted of two stages with stratification. Stands were chosen with probability proportional to size in the first stage, and one plot selected with equal probability per selected stand in the second stage. Due to the self-weighing features of the design, the data was analyzed as a stratified simple random inventory because every sampling unit in the stratum had an equal chance of being selected.

Two plot designs were utilized: one for the riparian stratum identified in the Roseburg and Medford Districts, and one for all other strata. The most commonly used design consisted of a two-acre area where all yew trees with a diameter greater than one-inch at breast height were recorded and several additional plots of different sizes were co-located within the two-acre area. There were four 1/10-acre plots for all live and dead trees greater than five inches, four 1/100-acre plots for all trees less than five inches, and a line transect for down logs within the two-acre plot. The riparian plot consisted of a half-acre where all yew one inch at breast height were recorded, and two 1/100-acre and a down-log transect with the same information recorded as for the larger plot.

Live yew one inch in diameter and larger was the basis for the yew analysis. Yew bark yields per tree were supplied by Hauser North-

west based on a single measurement at stump height. Diameters were recorded at DBH (diameter at breast height) for single stem trees. Diameters for multi-stem trees were recorded at DBH if the tree forked below DBH and above the fork for forks that occurred below the live crown. Forks that occurred within the crown were treated as a single-stem tree. Bark yields were based on the largest diameter and the tallest stem for multi-stem trees.

Trees were sorted by diameter within each of the three diameter classes. Leave trees within each class were the smallest trees and progressed towards the larger diameters until either the criterion for that class was met or all of the trees were left, whichever was reached first. One-inch trees qualified as leave trees, even though they were classified as sub-merchantable.

Modeling Process

Modeling of the alternatives was done in a fashion similar to the modeling procedures used by Region Six and Mason, Bruce and Girard. The basic plot data was processed using data base software, with the summary tables for the alternative outputs generated by a Lotus spreadsheet.

An important difference between the modeling methods used by the BLM and the Forest Service (Region Six) is that the BLM modelled harvesting at the individual plot level, while Region Six grouped their plots into averages per stratum and modelled harvesting at that level. While the mechanics of this may be unclear to the reader, the significance lies in the fact that the method used by the BLM is probably slightly better at determining which trees would be cut and which ones would be left. The stocking variation formed between plots is more pronounced at the plot level than at the average trees per stratum level, and thus may result in more instances where at the plot level, harvesting could not occur and still meet minimum leave tree requirements.

Results

The following tables display the results of modeling the alternatives using the inventory data from the BLM.

All Bureau of Land Management (BLM) Districts							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	2,032,678	2,084,678	0	0	0	0	0
B	2,032,678	2,084,678	62,400	43,884	22-33	247,102	124-185
C	2,032,678	2,084,678	680,973	105,157	53-79	714,842	357-536
D	2,032,678	2,084,678	680,973	162,744	81-122	922,356	461-692
F	2,032,678	2,084,678	680,973	255,194	128-191	1,374,970	687-1,031
G1	2,032,678	2,084,678	680,973	218,161	109-164	1,502,898	751-1,127
G2	2,032,678	2,084,678	1,406,614	449,450	225-337	3,243,270	1,622-2,432
*Trees >1" DBH							

Salem District							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	369,912	340,763	0	0	0	0	0
B	369,912	340,763	10,225	9,718	5-7	33,100	17-25
C	369,912	340,763	117,058	29,565	15-22	130,089	65-98
D	369,912	340,763	117,058	46,072	23-35	182,482	91-137
F	369,912	340,763	117,058	72,125	36-54	234,402	117-176
G1	369,912	340,763	117,058	58,006	29-44	242,076	121-182
G2	369,912	340,763	281,029	125,990	63-94	527,192	264-395
*Trees >1" DBH							

Eugene District							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	302,293	105,794	0	0	0	0	0
B	302,293	105,794	7,850	2,596	1-2	51,852	26-39
C	302,293	105,794	92,306	2,773	1-2	53,927	27-40
D	302,293	105,794	92,306	2,817	1-2	54,331	27-41
F	302,293	105,794	92,306	6,480	3-5	211,058	106-158
G1	302,293	105,794	92,306	11,850	6-9	261,933	131-196
G2	302,293	105,794	260,520	33,201	17-25	686,998	343-515
*Trees >1" DBH							

Roseburg District							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	390,967	846,647	16,725	0	0	0	0
B	390,967	846,647	139,260	26,920	13-20	139,575	70-105
C	390,967	846,647	139,260	66,009	33-50	491,762	246-369
D	390,967	846,647	139,260	105,389	53-79	640,429	320-480
F	390,967	846,647	139,260	156,261	78-117	835,959	418-627
G1	390,967	846,647	139,260	124,972	62-94	871,870	436-654
G2	390,967	846,647	309,648	242,255	121-182	1,762,387	881-1,322
*Trees >1" DBH							

Coos Bay District							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	309,018	41,630	11,490	0	0	0	0
B	309,018	41,630	138,684	1,152	1	7,669	4-6
C	309,018	41,630	138,684	2,235	1-2	14,115	7-11
D	309,018	41,630	138,684	3,319	2	17,073	9-13
F	309,018	41,630	138,684	6,569	3-5	29,965	15-22
G1	309,018	41,630	138,684	6,352	3-5	42,028	21-32
G2	309,018	41,630	246,086	13,275	7-10	87,771	44-66
*Trees >1" DBH							

Medford District							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	612,424	743,319	16,110	0	0	0	0
B	612,424	743,319	157,669	3,498	2-3	14,905	7-11
C	612,424	743,319	157,669	4,574	2-3	24,949	12-19
D	612,424	743,319	157,669	5,148	3-4	28,041	14-21
F	612,424	743,319	157,669	13,759	7-10	63,588	32-48
G1	612,424	743,319	157,669	16,981	8-13	84,993	42-64
G2	612,424	743,319	273,335	34,729	17-26	178,922	89-134
*Trees >1" DBH							

Lakeview District							
Alternatives	Total Acres Inventoried	Total Number of Trees on Inventoried Acres*	Acres Entered by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs)	Trees Harvested by this Alternative (next 5 yrs) 50%-25% reduction (M)	Pounds of Dry Bark (next 5 yrs)	Pounds of Dry Bark (next 5 yrs) 50%-25% reduction (M)
A	48,064	6,525	0	0	0	0	0
B	48,064	6,525	0	0	0	0	0
C	48,064	6,525	0	0	0	0	0
D	48,064	6,525	0	0	0	0	0
F	48,064	6,525	0	0	0	0	0
G1	48,064	6,525	0	0	0	0	0
G2	48,064	6,525	0	0	0	0	0

*Trees >1" DBH

State and Private Lands

State and private lands are not included in the management area covered by this EIS. However, this information is presented as an additional resource and for comparison with inventory data from public lands.

Congress has mandated that the Forest Service supplement its own and other federal agencies' inventories with estimates of natural resources on state and private lands. In Region Six, these inventories are performed by the Forest Inventory and Analysis Group (FIA) of the Pacific Northwest Research Station (PNW). The inventories are ongoing low-intensity samples that include many different species, including Pacific yew.

The following table shows the number of yew trees that are estimated to exist on state and private lands in California, Oregon, and Washington.

Number of Pacific Yew on State and Private Lands in California, Oregon, and Washington

Location	Diameter Class					
	1.0-4.9	5.0-10.9	11.0-14.9	15.0-20.9	21.0+	Total
California:						
North Coast	0	984,000	0	0	12,000	996,000
Sacramento	792,000	191,000	56,000	0	0	1,039,000
Total	792,000	1,175,000	56,000	0	12,000	2,035,000
Oregon:						
Northwest	1,133,000	68,000	182,000	0	0	1,383,000
West Central	681,000	98,000	145,000	54,000	0	978,000
Southwest	1,030,000	289,000	152,000	0	0	1,471,000
Blue Mountains	131,000	266,000	0	0	0	397,000
Total	2,975,000	721,000	479,000	54,000	0	4,229,000
Washington:						
Puget Sound	2,179,000	513,000	34,000	0	0	2,726,000
Olympic Peninsula	601,000	369,000	50,000	0	0	1,020,000
Total	2,780,000	882,000	84,000	0	0	3,746,000
Total All Three States	6,547,000	2,770,000	619,000	54,000	12,000	10,010,000

Sustainable Yield Calculation

The alternatives that have been proposed utilize an uneven flow harvest scenario in order to meet the projected demand level for taxol. During the scoping period, an interest was expressed in ensuring that yew harvest occur on a sustained-yield level. To make a true calculation of what could be harvested on a continued basis, it is necessary to estimate the number of existing trees and make an estimate of how much those trees will grow in the future. While the inventories that were taken give us a good idea of how many trees would be available for harvest, growth information was recorded only by the BLM.

In order to provide an approximation of how much bark could be obtained over an extended period of time at a sustainable level, the number of harvestable trees was divided by a rotation length that was estimated could produce a tree that could be harvested for bark (100 years). It was assumed that the first areas harvested would regenerate and be ready for a second harvest in 100 years. Because these trees would probably be smaller than the current existing stand, we would expect a smaller bark harvest in future rotations. This method gives a conservative estimate of how many trees could be available because no provisions are made for including growth information from the existing stand.

The following table shows the estimated harvest for the sustained yield, or more appropriately termed, even flow harvest.

Sustainable Yield Calculations		
Area	**Trees**	**Thousand Pounds of Dry Bark**
Region-6	162 M	1,271 M
BLM	10 M	61 M
Region-1	31 M	152 M
Total	203 M	1,484 M

Appendix G

Insects and Diseases of Pacific Yew

Appendix G

Insects and Diseases

Introduction

Information on arthropods and plant diseases found on any of the seven known species of the genus *Taxus* is scarce and widely scattered in the literature; as scattered as the various species of yew.

Insects

Based upon a brief review of the world literature on *Taxus,* it is suggested that the following types of arthropods are likely to be found:

- Gall-forming mites (Eriophyidae) and flies (Cecidomyiidae)
  --*Taxomyia taxi,* artichoke gall midge
  --*Cecidophyopsis psilaspis, Taxus* bud mite
  --*Nalepella tsugifoliae,* a needle-feeding mite of hemlock, is also found on yew

- Root-weevils (Curculionidae)
  --*Nemocestes incomptus,* woods weevil
  --*Otiorhynchus ovatus,* strawberry root weevil
  --*O. rugosostriatus,* rough strawberry root weevil
  --*O. rugifrons*
  --*O. sulcatus,* black vine weevil (*taxus* weevil)
  --*Sciopithes obscurus,* obscure root weevil

- Foliage feeders (Scarabaeidae, Curcolionidae, Torticidae)

- Mealybugs (Pseudococcidae)
  --*Dysmicoccus wistariae, Taxus* mealybug
  --*Pseudococcus affinis,* obscure mealybug
  --*P. comstocki,* Comstock mealybug
  --*P. longispinus,* longtailed mealybug
  --*P. maritimus,* grape mealybug

- Scales (Coccidae, Diaspididae)
  --*Aspidiotus nerii,* oleander scale
  --*Chrysomphalus dictyospermi,* dictyospermum scale
  --*Fiorinia externa,* elongate hemlock scale
  --*Parthenolecanium fletcheri,* Fletcher scale
  --*Pseudaulacaspis cockerelli,* false oleander scale
  --*Pulvinaria floccifera,* cottony *Taxus* scale
  --*Aonidiella taxus,* the Asiatic red scale

Diseases

Root Diseases

Diseases of Pacific yew have not been studied or reported in detail, but yew seedlings in the eastern United States have been damaged by the following root-infecting fungi:

--*Rhizoctonia solani,* damping-off
--*Phytophthora cinnamomi,* Phytophthora root rot
--*Pythium* species, damping-off

Older yew trees in the west have been reported as hosts for:

--*Armillaria* spp., Armillaria root disease
--*Phaeolus schweinitzii,* Schweinitzii butt rot
--*Phytophthora lateralis,* Port-Orford-cedar root disease

Stem Decays

Several species of fungi causing decay of the heartwood, have been identified in Pacific yew:

--*Phellinus nigrolimitatus,* big white pocket rot
--*P. robustus,* robustus trunk rot
--*P. pini,* red ring rot
--*Fomitopsis rosea,* brown top rot

Foliage Diseases

Several species of blight fungi have caused localized damage to Pacific yew foliage that has remained under snow for long periods of time:

--*Neopeckia coulteri,* brown felt blight
--*Herpotrichia juniperi,* brown felt blight
--*Phacidium taxicolum,* snow blight
--*Phacidium dearnessii,* snow blight

The following fungi, causing needle blights of yew, have been reported:

--*Asteridiella pitya,* black mildew
--*Dothiora taxicola,* needle-and shoot-blight
--*Macrophoma taxi,* yew leaf blight
--*Mycosphaerella taxi, (Septoria)*
--*Sphaerulina taxi,* yew leaf scorch
(*Sphaerulina taxi* causes the upper surface of the needle to become brown, giving the foliage a scorched appearance)

Stem Cankers

A few stem- or twig-infecting fungi, causing stem cankers, have been reported on Pacific yew:

--*Phyllostictina hystrella,* shoot and leaf blight
--*Diplodia taxi*

Appendix H

Pacific Yew Plant Associations

Appendix H

Plant Associations

Plant Associations

Pacific yew is extremely variable in growth form, in taxol content, and in the environmental settings in which it grows. It follows that the species should be present in an extremely large number of plant associations (a grouping of plant species that recur across the landscape within particular environments). In western Oregon, yew trees or shrubs can be found somewhere in almost every dry land forest plant association, although in some cases yews may occupy microsites that should not be considered part of the general association surrounding them.

Yew also occurs in some areas that could be classified as nonforest: avalanche chutes in which yew shrubs form dense thickets (Deevy, 1991), chaparral-like thickets of yew shrubs in the mountains of northern Montana, talus and scree slopes in which yew is the only tree present, and rocky cliffs. A parallel to the latter is *T. baccata* which grows on chalk cliffs in Cumbria in the British Isles (Bolsinger, 1988-91; Hartzell, 1991).

In the Dog Island National Recreation Area of coastal Alaska, Pacific yew occurs at sea level in boggy sites in association with Alaska cedar, mountain hemlock, western hemlock, and shore pine. This seems entirely uncharacteristic; yew seems to shun poorly drained soil elsewhere (Alaback and Juday, 1989).

Inventory plots on non-federal lands in Oregon and Washington show Pacific yew growing in 35 plant associations. In national forests in Oregon and Washington, excluding the Rogue River, Siskiyou, and Umpqua National Forests in southwest Oregon, Forest Service ecologists found yew in 37 plant associations, including some found on non-federal lands.

Yew occurred in 40 plant associations on the Siskiyou and west half of the Rogue River National Forests, and in 40 plant associations on the Umpqua and east half of the Rogue River National Forests. Yew occurred in eight plant associations in the Blue Mountains, nine associations in the Sierra Nevada and southern Cascades of California, and in 10 plant associations in the Oregon Coast range. On inventory plots on non-federal lands in northern California, yew was found in seven plant associations. Yew was observed on the Six Rivers National Forest in an additional association.

In Idaho and Montana, Pacific yew is found in 29 associations (terminology differs between regions; associations in Region Six are equivalent to series/habitat and type/phase in Region One).

Distribution and Habitat of Pacific yew in Northern Sierra Nevada and Southern Cascades of California (Fites, 1992)

Pacific yew occurs in scattered locations throughout the central and northern Sierr'a Nevada and southern Cascade mountains in California. This summary of the distribution and habitat of the Pacific yew is restricted to the Eldorado, Tahoe, Plumas, and Lassen National Forests, where ecology plot data was collected to classify mixed conifer forests. Obligate riparian vegetation was generally not sampled as part of this classification effort.

Within this geographic area, Pacific yew occurs primarily within the mixed conifer zone, between 3,000 and 5,000 feet. Trees were found in several plant associations including *Mcn-Lide2-Conu2 / Cococ, Mcn-Lide2-Conu2, Mcn-Acma / Cococ, Mcn-cma / Adbi, Mcn-Conu2 / Cococ, Mcn-Conu2 / Adbi-Diho2, and Mcn / Cococ / Adbi.* In addition, Pacific yew seedlings or saplings but not trees, were also found in the following plant associations: *Mcn-Lide2 / Cococ* and *Mcn / Adbi*. All of these plant associations occur on wet or moist sites, typically with moderately deep to deep soils. Soils are typically fine textured. Sites tend to be north or east-facing, and on lower slopes or near or at drainages. All of the primary indicator species indicate high moisture conditions. In this area, *Lide2* indicates high precipitation, *Acma* indicates high surface or subsurface water, *Conu2* indicates moist soils and cooler, moist air, *Cococ* indicates the same as *Conu2* but tends to occur more specifically near running water, and *Adbi* indicates moist soils. The highest frequencies of Pacific yew are in the *Mcn-Lide2-Conu2* (41 percent) and *Mcn-Conu2 / Cococ* (62 percent), suggesting that moist but well drained soils are characteristic. Most of these plant associations have a high proportion of Douglas-fir in the tree layers, further indicating a tendency toward the moister, cooler environments in the mixed conifer zone.

The habitat of Pacific yew in the northern Sierras and southern Cascades can be characterized by its plant community affiliations as: moist to wet soils, cool and humid air, and typically north-facing lower slopes or drainages. Seedlings are sometimes observed on mid-slopes, but not trees, indicating less suitable habitat. The highest densities of Pacific yew have been observed on fine-textured alluvial soils, and on flat alluvial terraces or benches. In the northern Sierra Nevada and southern Cascades, Pacific yew is almost always associated with riparian environments, occurring near or at water sources. When the plant associations occur near seasonal, or more commonly year-around water sources, Pacific yew is often present. The *Mcn-Conu2/Cococ* has the highest frequency of Pacific yew and usually occurs near or at water sources. It seems likely that the other plant associations are not obligate riparian plant communities, but their affiliation with moist, cool, humid environments results in their common occurrence in these areas. Other sites away from riparian environments can also provide sufficient combinations of these factors for the common species in these plant associations but typically not Pacific yew.

One other factor that is important in characterizing the habitat of Pacific yew in California is that it is considered somewhat of a relic species. Some of its limited distribution may be explained by the past constriction of its distribution under different climatic conditions of earlier geologic eras.

The Following is a List of Plant Associations Where Yew Is Found:

Plant Associations With Yew Present in the Northern Rocky Mountains (Idaho and Montana)

Tabr/Asca	Pien/Clun	Tshe/Gydr
Tabr/Clun	Pien/Clun/Vaca	Tshe/Asca/Mefe
Abgr/Clun	Abgr/Clun	Abla/Opho
Abgr/Asca	Abgr/Arnu	Abla/Clun
Abgr/Asca/Mefe	Thpl/Clun	Abla/Clun/Arnu
Abgr/Asca/Tabr	Thpl/Arnu	Abla/Clun/Vaca
Abgr/Asca/Asca	Thpl/Mefe	Abla/Clun/Xete
Abgr/Libo	Thpl/Opho	Abla/Clun/Mefe
Abgr/Setr	Tshe/Clun	Abla/Libo/Xete
Abgr/Xete	Tshe/Clun/Arnu	

Plant Associations With Yew Present on Non-federal Lands in Northern California

Psme/Lide/Quch	Abco/Lide/Chum	Chla
Abco/Acma/Acci	Sese/Vaov	
Abco/Lide/Chfo	Sese/Pomu	

Plant Associations With Yew Present in Western Oregon and Washington North of the Umpqua National Forest
(National Forests and non-Federal lands)

Psme/Bene	Tshe/Rhma-Vaal/Coca	Tshe/Vaal/Oxor
Psme/Hodi/Grass	Tshe/Rhma/Xete	Tshe/Pomu-Oxor
Psme/Hodi/Whmo	Tshe/Rhma/Bene	Tshe-Psme/Hodi
Psme/Gash	Tshe/Rhma/Oxor	Tshe/Titr
Abgr/Bene	Tshe/Rhma-Gash	Abam/Tiun
Abam-Abgr/Smst	Tshe/Rhma/Libo2	Abam/Actr-Clun
Tshe/Bene	Tshe/Gash	Abam/Bene
Tshe/Bene/Oxor	Tshe/Pomu	Abam/Gash
Tshe/Bene-Gash	Tshe/Libo2	Abam/Vaal-Gash
Tshe/Bene/Actr	Tshe/Actr	Abam/Mefe
Tshe/Opho	Tshe/Conu/Actr	Abam/Vame/Clun
Tshe/Oxor	Tshe/Opho/Pomu	

Plant Associations With Yew Present in Mount Rainier National Park

Moist Sites	Dry Sites	Cold Sites
Tshe/Pomu	Tshe/Gash	Abam/Rula - Rula phase
Tshe/Actr	Psme/Vise	
Tshe phase	Abam/Gash	
Abam phase	Abam/Bene	
Tshe/Opho	Abam/Xete - Tshe phase	
Abam/Opho		
Valley phase		
Slope phase		
Abam/Tiun - Climax phase		

Plant Associations with Yew Present in the Blue Mountains
(of Northeastern Oregon)

Abgr/Tabr/Clun	Abgr/Tabr/Libo2	Abgr/Pomu-Asca3	Abgr/Trca3
Abgr/Gydr	Abgr/Acgl	Abgr/Clun	Abgr/Libo2

Plant Associations With Pacific Yew Present in the Umpqua and East Half of the Rogue River National Forests
(Southern Oregon Cascades Geological province)

Abco-Tsme	Psme/Rhdi	Tshe/Bene/Actr
Psme/Bene/Pomu	Tshe-Abam	Tshe/Gash/Pomu
Psme-Abmas/Bene	Tshe/Pimo/Vame	Abam-Tshe
Psme/Abam	Tshe/Vame/Oxor	Abam/Acci/Titr
Psme/Vame/Actr	Tshe/Bene/Oxor	Abam-Thpl/Runi
Psme/Runi/Actr	Tshe/Gash/Oxor	Tshe-Thpl/Rhma
Psme/Amal/Ande	Tshe/Acgl/Smst	Tshe-Thpl/Bene
Psme/Tshe-Acci	Tshe/Acci-Alru	Tshe-Thpl/Conu
Psme/Acci/Actr	Tshe/Cade3/Rhma/Clun	Tshe-Thpl/Oxor
Psme/Acgl/Bene	Tshe/Tabr/Rhma	Tshe-Thpl-Psme
Psme/Bene-Gash	Tshe/Rhma/Libol	Thpl-Tshe/Rhma
Psme/Chumn/Libol	Tshe/Gash/Libol	Thpl-Tshe/Whmo
Psme/Cade3/Bene	Tshe/Gash/Hial	
Psme/Psme/Bepi	Tshe/Bene/Libol	

Plant Association With Pacific Yew Present in the Siskiyou and West Half of the Rogue River National Forests
(Klamath Geological Province)

Abco-Tabr	Tshe-Abam	Psme/Bene/Pomu
Abco-Abmas/Bene	Tshe-Pimo/Vame	Psme/Gash/Pomu
Abco-Abam	Tshe/Vame/Oxor	Abam-Tshe
Abco/Vame/Actr	Tshe/Bene/Oxor	Abam-Acci/Titr
Abco/Runi/Actr	Tshe/Gash/Oxor	Tshe-Thpl/Runi
Abco/Amal/Ande	Tshe-Acgl/Smst	Tshe-Thpl/Rhma
Abco-Tshe-Acci	Tshe-Acci-Alru	Tshe-Thpl/Bene
Abco/Acci/Actr	Tshe-Cade3/Rhma/Clun	Tshe-Thpl/Conu
Abco-Acgl/Bene	Tshe-Tabr/Rhma	Thse-Thpl/Oxor
Abco/Bene-Gash	Tshe/Rhma/Libol	Tshe-Thpl-Psme
Abco/Chumn/Libol	Tshe/Gash/Libol	Thpl-Tshe/Rhma
Abco-Cade3/Bene	Tshe/Gash/Hial	Thpl-Tshe/Whmo
Abco-Psme/Bepi	Tshe/Bene/Libol	
Abco/Rhdi	Tshe/Bene/Actr	

Plant Associations with Pacific Yew in the Northern Sierra Nevada and Southern Cascades of California

Mcn-Acma/Adbi	Mcn-Acma/Cococ	Mcn-Conu2/Adbi/DiHo2
Mcn-Conu2/Cococ	Mcn/Cococ/Adbi	Mcn-Lide2-Conu2
Mcn-Lide2-Conu2/Cococ	Mcn-Lide2/Cococ	Mcn/Adbi

Plant Associations with Pacific Yew Present in the Oregon Coast Range

Tshe/Oxor	Tshe/Bene-Gash	Pisi/Rusp-Gash	Pisi/Oxor
Tshe/Acci-Gash	Tshe/Bene	Tshe/Vaov2	Tshe/Rhma/Pomu
Tshe/Rhma-Bene	Tshe/Rhma-Vaov2		

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Appendix I

Soils

Appendix I

Soils

SOILS

Oregon, Washington, Montana and Idaho can be divided into generalized physiographic provinces. (Fenneman, 1931; Arnold, 1974; Franklin & Dyrness, 1973; Boyer & Rich, Unpublished, 1978). These provinces are characterized by their geologic origin and shape as well as erosional, depositional, and mountain building processes. Understanding some of the processes that help shape the landscape provides insight into predicting human activities on the landscapes. Processes themselves are not phenomena, but are the interactions of different elements over time. For instance, past climatic conditions produced erosional forces (sculpturing) and deposition that created existing landforms. The impact of erosional forces depends upon the original geology of the area - whether the parent material was hard or soft, and so on. Biological communities, in turn, are influenced by the interaction of annual climatic patterns and existing landforms. Changes in any of these elements alter other elements through interaction. Resource management (as in Pacific yew harvest activities) produce changes in the biological community that may influence the landform and the relative impact of climate on the site.

Olympic Province

The major portion of this Province exhibits extensive glaciation. Main river valleys are broad and U-shaped. Major peaks are ringed with cirques (circular spaces) and many contain active glaciers. Extremely high precipitation has caused rapid downcutting by streams and, with past glacial erosion, has created steep mountain slopes. These rugged mountains provide a central core surrounded by almost level lowlands which are a result of glacial action. The Province has a very moist marine climate, one of the wettest annually in the continental United States (over 200 inches). Most precipitation occurs as rain except at higher elevations, where snow dominates. Due to the heavy snowfall, glaciers are common at the upper elevations. Heavy summer rains are also common. Two major runoff periods occur, spring and late fall. Typical vegetation includes extremely dense stands of Douglas-fir, western hemlock, and western redcedar, with Sitka spruce along the western edges (the Pacific Coastline). Soils in the Sitka spruce community are medium to coarse textured, and shallow to moderately deep. In the hemlock and subalpine zones they are medium textured, and shallow to moderately deep.

Coast Range Province

This Province contains steep mountain slopes with ridges that are often extremely sharp. The ridge system is usually parallel to the coast, but is dissected so much that this may not be readily apparent. The topography varies as well. The dunal area is nearly level with steep lands along the eastern edges. Scattered, often barren peaks rise well above surrounding ridges. The Province has a moist marine climate with annual precipitation of 60 to 120 inches. Most of this occurs as rain. Late fall floods are common and summers and winters are relatively mild. One major runoff period usually occurs in late fall or early winter. Vegetation is characterized by Sitka spruce, western hemlock, western redcedar, Douglas-fir, grand fir, and red alder. Soils are medium textured and shallow to moderately deep at the lower elevations, and close to the coastal fog zone. Further inland and upslope, medium to fine textured and moderate to deep soil mantles predominate. Sandstones, basalts, and other volcanic materials are common to this province.

Yew is rare in the Coast Range between the Quinault Indian Reservation in Washington and the Umpqua River in Oregon. It is much more abundant east of Interstate 5 in the lowlands and foothills of the Cascades.

Siskiyou Province

This province is found in northern California and southern Oregon and exhibits an ancient, and now greatly dissected, uplifted plain. Some peaks, however, rise above the generally even ridge. The province has a moist marine climate with annual precipitation (mostly rain) of 45 to 90 inches. Late fall floods are common, summers are warm and dry, and winters are relatively mild. Vegetation reflects elements of the northern California coast and southern Oregon flora, with many species indigenous only to the Siskiyou character type. Major plant communities are distributed in relation to moisture and elevation and include: Pine-oak-fir, fir-broadleaved species, pine-fir-cedar-true firs, white fir, Shasta red fir, western hemlock, and Sitka spruce. This diversity combines with a long history of disturbance, primarily fire, to produce an extremely varied array of biological communities. Soils are generally medium textured and moderately deep to deep. Large areas of serpentine and periodotite bedrock are common to this province.

Puget Sound

This Province was subjected to massive continental glaciation, which formed an area of low relief broken by sounds, low moraine ridge systems, rounded hummocks, and many included lakes. The Province has a moist marine climate with annual precipitation (mostly rain) of 15 to 60 inches. Peak runoff generally occurs in late fall to early winter. Vegetation is characterized by Douglas-fir, Sitka spruce, western hemlock, western redcedar, and grand fir. Some stands of lodgepole pine are found on moraine remnants.

Western Cascades Province

This Province is composed of a slightly folded and uplifted accumulation of weathered volcanic flows. The area is characterized by a general conformity in ridge crests separated by deep valleys with steep, highly dissected side slopes. In the southern portion of this Province, major valleys are "V-shaped", indicating a strong water-erosion process rather than glacial scouring. Glacial features are evident but not pronounced throughout the entire Province. Climate is similar to the northeastern Cascades but with slightly warmer temperatures and lower annual precipitation (about 130 inches). The major runoff period is usually late fall to early winter. Vegetation is characterized by Douglas-fir, western hemlock, grand fir, and subalpine fir. Mixed conifer and subalpine zones are also found in this province. Soils in the hemlock zone are generally fine textured and deep, while in the mixed conifer zone they are medium textured and moderately deep. In the oak woodlands vegetation zone they are fine textured and moderately deep, and in the subalpine zone they are medium to coarse textured and moderately deep.

Northwestern Cascades Province

This province is characterized by sharp, jagged peaks and deep valleys resulting mostly from alpine glaciation. A striking topographic feature is the approximately uniform elevation of the main ridgetops. Towering above these relatively even crests are two dormant volcanoes (Mt. Baker and Glacier Peak) as well as several granitic peaks of exceptional height. Main stream valleys contain deep accumulations of glacial debris. This is an area of heavy annual precipitation (from 80 to 160 inches), much of which occurs as snow. The climate is noted

for high humidity and relatively mild temperatures. Both late fall floods from rain and high summer streamflows from glacier melt are common. Vegetation is characterized by western hemlock, Douglas-fir, and western redcedar. Subalpine fir, noble fir, and Pacific silver fir occur at higher elevations. In the hemlock zone the soils are medium to coarse textured and moderately deep. In the subalpine zone they are medium textured and generally shallow.

Recent (high) Cascades Province

This province consists of a volcanic plateau capped by shield volcanoes, cinder cones, and other volcanic forms - all of which are in various stages of disintegration. It is essentially an area of gently sloping terrain, interrupted at intervals by glaciated channels in the major drainages. The area is dotted with volcanic peaks and cones rising 150 to 5000 feet above the surrounding landscape. Much of the area is mantled with pumice and volcanic ash. It is an area of climatic extremes. In Washington, annual precipitation ranges from 15 inches on the eastern edge to 140 inches at the crest of the Cascades. Summer is characterized by low humidity and little rain. The major source of streamflow is from snowmelt with peak flows occurring in late spring. In southern Oregon, annual precipitation ranges from 20 to 60 inches, of which about 50 percent occurs as snow. This area is characterized by warm summers and relatively cold winters. High rainfall intensities associated with summer thunderstorms are common throughout the Province. Vegetation varies greatly in composition and includes: Douglas-fir, grand fir, subalpine fir, and western hemlock as well as ponderosa and lodgepole pine. In the hemlock and mixed conifer zones, soils are medium textured and moderately deep to deep. The subalpine zone is characterized by medium to coarse textured and generally shallow soils. In the Douglas-fir/grand fir (non-pumice soils) zone, they are medium to coarse textured and moderately deep to deep. The Douglas-fir/grand fir (pumice soils) zone soils are typically coarse textured and deep. In the ponderosa pine/lodgepole (non-pumice) zone, soils are medium to coarse textured and moderately deep, while in the ponderosa pine/lodgepole (pumice soils) zone, they are coarse textured and moderately deep to deep.

Modoc Plateau (Upper Basin and Range Province)

This Province exhibits fault-block mountains. Most of the enclosing basins, surrounded by lifted blocks, are internally drained. These formations create predominantly horizontal profiles in mountain silhouette with occasional cone-shaped features. Annual precipitation is moderate (15 to 30 inches) and occurs mostly as snow. Most streams are perennial (flow throughout the year) and many undrained basins contain shallow lakes and marshes. High intensity precipitation from summer thunderstorms is common. Peak streamflows occur in the spring.

Vegetation is characterized by mixed conifer, ponderosa pine, lodgepole pine, and grass-shrub communities. In the Douglas-fir/grand fir (non-pumice) soils, the soil textures are generally medium to coarse and moderately deep. In the Douglas-fir/grand fir (pumice) soils, the soils are coarse textured and moderately deep to deep. The ponderosa pine/lodgepole pine (non-pumice soils) communities are typically medium to coarse textured and moderately deep, while the ponderosa pine/lodgepole (pumice soils) zones are coarse textured and moderately deep to deep.

Sierra Nevadas

This province is characterized by a block mountain range that is tilted to the west, with evenly crested ridges and alpine peaks near the east side. Deep river-cut canyons occur on the western slopes while at their upper reaches, especially in massive granites of the higher Sierras, the canyons are modified by glacial sculpturing. Glacial moraines and alluvial fans spread over fault rifts and dropped blocks along the eastern base of the range. Metamorphic bedrock (capped by volcanics) predominates the western flank and northern end of the Sierras.

Vegetation varies with elevation and also in the rain shadow on the easterly flanks of this range. On the westerly flanks, oak brush gives way to mixed conifer predominated by pine. This grades from mixed pine/oak to a true mixed conifer zone with pine and Douglas-fir. Above this elevation is an area of true fir and finally above timberline, low brush and barrens.

Northeastern Cascades

This Province exhibits glacial sculpturing which has created an area of great relief with steep-sided, very deep valleys and long finger lakes. The area is made of granitic batholiths (folded and, in part, metamorphosed) and sedimentary rock with ridgetops having approximately uniform crest elevations. An area of climatic extremes, annual precipitation ranges between 20 to 120 inches, most of which occurs as snow. Peak water flows occur in late spring and early summer. Summer temperatures are very hot. High rainfall intensities associated with summer thunderstorms are common. Vegetation is characterized by a wide range of species, including subalpine fir, grand fir, Douglas-fir, and western larch, as well as some ponderosa and lodgepole pine.

Okanogan Highland Province

This province reflects repeated continental glaciation, resulting in a generally rolling terrain of moderate slopes and broad, rounded summits. Scattered peaks rise 3,000 to 4,000 feet above the general terrain, dividing the area into several upland areas separated by a series of broad north-south valleys. Annual precipitation ranges from 20 to 45 inches. A continental-type climate prevails here with cold winters and warm summers, and high summer rainfall intensities. Peak runoff occurs in mid-spring. Vegetation is characterized by grand fir and Douglas-fir with larch and ponderosa pine. In the subalpine and the Douglas-fir/grand fir (non-pumice soils) zone and in the Ponderosa pine/lodgepole pine (non-pumice soils) zone, the soils are medium to coarse textured and moderately deep.

Blue Mountains Province

This province is composed of several ranges of mountains separated by faulted valleys, synclinal (downfolded) basins, canyon lands, and lava plateaus. Topographic relief in the mountains is highly variable with moderately steep sideslopes common. Dissection of the lava plateaus has also created steep side slopes. Most of the area is blanketed by volcanic ash from the Mt. Mazama eruption. Climate is more typical of the continental type, with annual precipitation ranging from 15 to 60 inches, much of which occurs as snow. Peak runoff occurs in the spring. The province has relatively cold winters and warm summers with wide diurnal temperature fluctuations. Summers typically have low humidities. Vegetation is characterized by ponderosa pine, grand fir, Douglas-fir, some subalpine fir communities, and shrub-grass communities. The soils are medium textured and moderately deep to deep in the subalpine and Douglas-fir/grand fir (non-pumice soils) zones, and medium to fine textured and moderately deep in the ponderosa pine/lodgepole pine (non-pumice soils) zone.

Wallowa Province

This province consists of a mountainous "island" surrounded by lava plateaus. These mountains are part of the Blue Mountain Province but are distinctive, since alpine glaciation has created a very precipitous and ruggedly mountainous area; relief is much greater than in the Blue Mountains type. Climate is similar to the Blue Mountains Province except that the Wallowas have higher annual precipitation, ranging from 25 to 80 inches (primarily caused by the higher elevations). Rainfall intensities are greater and temperatures are colder than in the Blue Mountain Province. Peak runoff occurs in late spring or early summer. Vegetation is characterized by grand fir, Douglas-fir, subalpine fir, mountain hemlock, and ponderosa pine. In the Douglas-fir/grand fir (non-pumice soils) plant community, soils are medium textured and moderately deep. Climatic conditions in this area are characterized by warm, dry summers and cool, wet winters, with snow pack providing the major source of water after the early spring peak flow. Isolated thunderstorms are not uncommon during frontal passage in the summer months.

Soils grade from deep and well-developed to shallow, poorly developed granitic material at high elevations.

Northern Rocky Mountains Province - North Part

This province is found in northern Idaho and western Montana and is comprised of a number of mountain ranges. Most elevations are between 2000-9000 feet. The continental ice sheet extended into the northern part of the area and produced rounded and smooth topographic features. Glacial till, outwash, and lacustrine material can be found on the landscapes affected by glaciation. Alpine glaciers occurred at higher elevations throughout the province producing cirque basins on north and east aspects. South of the area affected by continental glaciation, the landscapes are largely residual with the regolith having formed by in-place weathering. These residual landscapes vary from being non-dissected to highly dissected and from weakly to highly weathered.

The major parent materials for the soils in this geomorphic unit include:

1. Belt Subgroup - located mainly east and southeast of Coeur d'Alene Lake to the Montana border and east of Pend Oreille Lake along the Montana border to the Canadian border. Rocks and weathered materials from rocks consist of gneisses, schists, amphibolites, and quartzites; shales and sandstones; some gabbro and diorite; and local silicic intrusives.
2. Glacial features - located mainly in the area from Coeur d'Alene Lake north to the Canadian border.
3. Columbia River Group - located mainly in the Coeur d'Alene Lake and Orofino areas.
4. Other minor formations such as metamorphic complexes, quartzites, shale, limestone, and conglomerates.

Volcanic ash from Mt. Mazama is found at the soil surface. The ash is thinner in the northern and eastern parts of the province. The climate is influenced by Pacific maritime air masses. Winters are cool and wet while summers are dry. Rain-on-snow events occur at mid to lower elevations during the winter on the western slopes only. Precipitation varies from about 15 inches at lower elevations to around 100 inches at

the highest elevations. Vegetation at higher elevations is mainly subalpine fir and Englemann spruce with some mountain hemlock. Mid-elevation sites commonly have western white pine, western redcedar, western larch, grand fir, and lodgepole pine. Western hemlock is important in the northwestern portion of the province. Douglas-fir and ponderosa pine occur at lower elevations and on dry aspects. Dry bunchgrass can be found in lower elevation river canyons in the southern part of the province. Most soils have a medium textured volcanic ash surface layer. The soils associated with granitics have coarse textured subsoils and substratums. Those associated with "Belt" rocks have medium textured or moderately coarse textured subsoils and substratums. The soils derived from glacial till frequently have very dense subsoils and substratums.

Northern Rocky Mountains Province - Central Part

This province is characterized by high mature mountains and deep intermontane valleys. About 10 percent of the landscape has been altered by alpine glaciation. Steep stream breaklands and colluvial slopes are almost 50 percent of the landscape. Broadly rounded ridges affected by periglacial activity are 17 percent, and dissected hills and rolling uplands are 28 percent.

The major parent materials for soils in this geomorphic unit include:

1. Idaho Batholith and related rocks - dominant formation found throughout the central part of the province.
2. Gneisses, schists, and quartzites; andesites and basalts.

Elevations range from 1000 to 8000+ feet, with a climate that is markedly different from the sections to the north. Mountain barriers impede the normal movement of moisture-laden air masses from the Pacific Ocean.

Soils in a large portion of the area are dominantly deep to moderately deep, with loamy sands to sandy loam textures. The influence of Aeolian (windborne) material tends to be masked by glacial, frost churning, and colluvial action. Ash deposits about one foot thick over well-weathered bedrock can be found in the Red River Basin subsection.

Habitat types are dominantly subalpine fir/beargrass, subalpine fir/whortleberry, with whitebark pine/subalpine fir on high knobs and rocky ridges. Douglas fir/beargrass is on lower elevation north slopes with Douglas fir/ninebark and Douglas fir/Agsp on south slopes.

Terminology

Soil mantle effective depths (rooting zone) are represented by three classifications: shallow, less than 20 inches; moderate, 20 to 40 inches; and deep, 40 inches or more. Three classes are also included for soil textures:

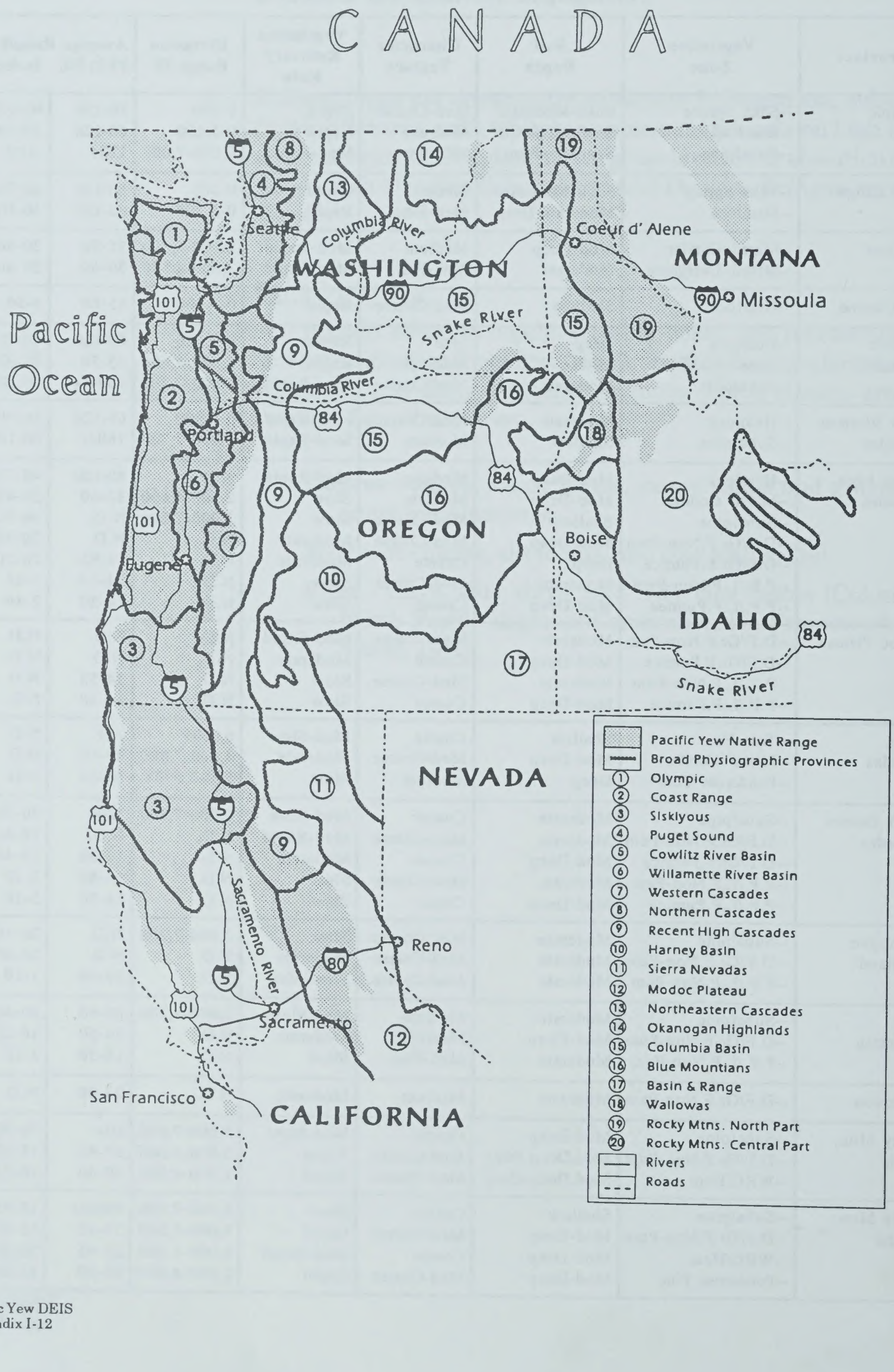
Coarse - sands, sandy loams, loamy sands and gravelly to stony combinations;

Medium - loams, silt loams, and clay loams; and

Fine - clays, silty clays, and silty clay loams (Columbia-North Pacific Regional Comprehensive Framework and Study, 1970).

Physiographic Provinces and Conditions							
Province	**Vegetation Zone**	**Soil Depth**	**Character Texture**	**Vegetation Recovery Rate**	**Elevation Range Ft.**	**Average PPT. IN.**	**Runoff Inches**
Olympic	--Sitka Spruce --Hemlock --Subalpine	Shall-Moderate Shall-Moderate Shall-Medium	Med-Coarse Medium Medium	Rapid Rapid Mod-Rapid	0-500 0-3,280 2,000-7,000	80-120 60-120 120+	95-105 80-100 -100
Coast Range	--Sitka Spruce --Hemlock	Shall-Moderate Moderate-Deep	Medium Med-Fine	Rapid Rapid	0-500 0-3,200	80-120 60-120	60-70 40-100
Siskiyou	--Mixed Conifer --Mixed Evergreen	Mod-Deep Moderate	Medium Med-Fine	Mod-Rapid Mod-Rapid	2,500-4,600 2,600-4,550	35-90 30-60	20-50 20-40
Puget Sound	--Hemlock	Shallow	Med-Coarse	Rapid	0-3,300	15-60	5-30
Western Cascades	--Hemlock --Mixed Conifer --Subalpine	Deep Moderate Moderate	Fine Medium Med-Coarse	Rapid Rapid Mod-Rapid	0-3,200 2,500-4,600 2,000-7,200	60-120 35-50 130+/-	40-70 20-40 60-100
North Western Cascades	--Hemlock --Subalpine	Moderate Shallow	Med-Coarse Medium	Mod-Rapid Mod-Rapid	0-3,300 2,000-7,200	60-120 160+/-	60-90 80-100
Recent High Cascades	--Hemlock --Mixed Conifer --Subalpine --D.F/Gr.F.Non-Pum --D.F/Gr.F.Pumice --P.P./L.P.Non-Pum --P.P./L.P.Pumice	Mod-Deep Mod-Deep Shallow Mod-Deep Deep Moderate Mod-Deep	Medium Medium Med-Coarse Med-Coarse Coarse Med-Coarse Coarse	Mod-Rapid Slow Slow Moderate Moderate Slow Slow	N.D. 2,500-4,600 2,000-7,200 N.D. N.D. N.D. N.D.	60-120 30-60 N.D. N.D. 14-30+ 14-30 14-30	40-70 20-40 30-70 20-30 10-20 5-10 2-10
Modoc Plateau	--D.F/Gr.F.Non-Pum --D.F/Gr.F.Pumice --P.P./L.P.Non-Pum --P.P./L.P.Pumice	Moderate Mod-Deep Moderate Mod-Deep	Med-Coarse Coarse Med-Coarse Coarse	Mod-Rapid Moderate Slow Slow	N.D. N.D. N.D. N.D.	N.D. N.D. 14-30 14-30	N.D. N.D. N.D. N.D.
Sierra Nevadas	--True Fir --Mixed Conifer --Ponderosa Pine	Shallow Mod-Deep Deep	Coarse Med-Coarse Medium	Mod-Slow Moderate Slow	6,000+ 4,000-7,000 500-3,500+	70+ 40-60 30-50	N.D. N.D. N.D.
North Eastern Cascades	--Subalpine --D.F/Gr.F.Non-Pum --D.F/Gr.F.Pumice --P.P./L.P.Non-Pum --P.P./L.P.Pumice	Moderate Moderate Mod-Deep Moderate Mod-Deep	Coarse Med-Coarse Coarse Med-Coarse Coarse	Mod-Slow Mod-Rapid Moderate Slow Slow	2,000-7,200 N.D. N.D. N.D. N.D.	120+ N.D. 14-30 14-30 14-30	40-70 10-40 10-40 5-10 5-10
Okanogan Highland	--Subalpine --D.F/Gr.F.Non-Pum --P.P./L.P.Non-Pum	Moderate Moderate Moderate	Med-Coarse Med-Coarse Med-Coarse	Slow Moderate Slow-Mod	2,000-7,200 N.D. N.D.	N.D. N.D. 14-30	20-40 10-20 1-10
Blue Mountain	--Subalpine --D.F/Gr.F.Non-Pum --P.P./L.P.Non-Pum	Moderate Mod-Deep Moderate	Medium Medium Med-Fine	Mod-Slow Moderate Slow	2,000-7,200 N.D. N.D.	40-60 30-50 14-30	20-40 10-20 2-10
Wallowas	--D.F/Gr.F.Non-Pum	Moderate	Medium	Moderate	N.D.	25-80	N.D.
Rocky Mtns. North	--Subalpine --D.F/Gr.F.Non-Pum --WRC/Hem	Mod-Deep Mod.Deep-Deep Mod.Deep-Deep	Coarse Med-Coarse Med-Coarse	Mod-Slow Rapid Rapid	5,000-7,000 3,000-6,000 2,000-4,000	60+ 35-60 30-40	30-50 15-30 10-25
Rocky Mtns. Central	--Subalpine --D.F/Gr.F.Non-Pum --WRC/Hem --Ponderosa Pine	Shallow Mod-Deep Mod-Deep Mod-Deep	Coarse Med-Coarse Coarse Med-Coarse	Slow Rapid Mod-Rapid Rapid	5,500-7,500 3,000-6,000 3,000-5,000 2,000-4,000	40-60+ 35-45 20-45 20-30	15-35 15-30 20-30 15-20

Figure I-1: Broad Physiographic Provinces



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Appendix J

Wildlife and Biological Assessment

Appendix J

Wildlife and Biological Assessment

Table of Contents Page(s)

Introduction

This appendix lists three types of wildlife: listed and proposed endangered and threatened species; proposed endangered and threatened species that may be affected by yew harvest; and other species of concern that may occur in yew habitat. Following these is an appended section with additional detail and background information on how yew harvest and the proposed alternatives could affect animals and special status plants, including the northern spotted owl.

List A

The following are listed and proposed endangered and threatened species that may occur in the area of the proposed harvesting of Pacific yew in Regions 1 and 6 of the U.S. Fish and Wildlife Service.

Threatened

Fish

Lahontan Cutthroat Trout *(Oncorhynchus clarki henshawi)*
Paiute Cutthroat Trout *(Oncorhynchus clarki seleniris)*
Foskett Speckled Dace *(Rhinichthys osculus ssp.)*
Warner Sucker *(Castostomus warnerensis)* {critical habitat}
Sacramento River Winter Chinook Salmon *(Onchorynchus tshawytscha)*
Snake River Fall Chinook Salmon *(Onchorynchus tshawytscha)*
Snake River Spring/Summer Chinook Salmon *(Onchorynchus tshawytscha)*

Birds

Marbled Murrelet *(Brachyramphus marmoratus)*
Northern Spotted Owl *(Strix occidentalis caurina)* {critical habitat}
Aleutian Canada Goose *(Branta canadensis leucopareia)*
Bald Eagle *(Haliaeetus leucocephalus)* {Oregon and Washington}

Mammals

Grizzly Bear *(Ursus arctos)*

Invertebrates

Oregon Silverspot Butterfly *(Speyeria zerene hippolyta)*
Valley Elderberry Longhorn Beetle *(Desmocerus californicus dimorphus)*

Endangered

Fish

Shortnose Sucker *(Chasmistes brevirostris)*
Lost River Sucker *(Deltistes luxatus)*
Borax Lake Chub *(Gila boraxobius)* {critical habitat}
Snake River Sockeye Salmon *(Onchorynchus nerka)*

Birds

Bald Eagle *(Haliaeetus leucocephalus)*
{California, Idaho, Montana}
American Perégrine Falcon *(Falco peregrinus anatum)*
California Brown Pelican *(Pelecanus occidentalis californicus)*

Mammals

Columbian White-tailed Deer
(Odocoileus virginianus leucurus)
Gray Wolf *(Canis lupus)*
Woodland Caribou *(Rangifer tarandus caribou)*

Plants

McDonald's Rock-cress *(Arabis mcdonaldiana)*
Bradshaw's Lomatium *(Lomatium bradshawii)*
MacFarlane's Four o'clock *(Mirabilis macfarlanei)*
Malheur Wire-lettuce *(Stephanomeria malheurensis)*

Proposed Species

Fish

Oregon Chub *(Oregonichthys (-Hybopsis) crameri)*

Birds

Western Snowy Plover *(Charadrius alexandrinus nivosus)*

Plants

Applegate's Milk-vetch *(Astragalus applegatei)*
Nelson's Sidalcea {Checker Mallow} *(Sidalcea nelsoniana)*
Marsh Sandwort *(Aranaria paludicola)*

List B

The following species (taken from the above list) may occur in yew habitat and/or may be affected by the harvest of Pacific yew. The effects of yew harvest on these species are analyzed in Chapter IV of this EIS. Species not listed below do not occur in yew habitat, nor will they be affected by yew harvest and are therefore not analyzed in this document.

Threatened Species

Sacramento River winter Chinook salmon

The Chinook salmon is found along the Pacific coast from the Ventura River in southern California to Point Hope, Alaska. It is also found in northeast Asia, from the Anadyr River to Hokkaido, Japan.

Juvenile Chinook salmon spend about a year in fresh water before smolting and migrating to the Pacific Ocean. Feeding fish remain in the ocean from 3 to 4 years (range, two to eight years) before they mature and return to their parent stream to spawn. Average egg production by a female is 5,000 (range 2,250-7,750). The eggs hatch in about two months, depending on water temperature. The young remain in the gravel two to three weeks after hatching. Juveniles remain in fresh water from a few days to three years.

It is unknown at this time if this species occurs in yew habitat. As more information comes in, this question will be answered.

Snake River fall Chinook salmon

The Chinook salmon is found along the Pacific coast from the Ventura River in southern California to Point Hope, Alaska. It is also found in northeast Asia, from the Anadyr River south to Hokkaido, Japan.

Juvenile Chinook salmon spend about a year in fresh water before smolting and migrating to the Pacific Ocean. Feeding fish remain in the ocean from three to four years (range, two to eight years) before they mature and return to their parent stream to spawn. Fall Chinook migrate in August and September and spawn as soon as the spawning grounds are reached, when water temperatures are between 42° and 58°F. Average egg production by a female is

5,000 (range 2,250-7,750). The eggs hatch in about two months, depending on water temperature. The young remain in the gravel two to three weeks after hatching. Juveniles remain in fresh water from a few days to three years. Usually, juvenile fall Chinook feed for a short time and then migrate to the ocean.

This species may be affected by yew harvest.

Snake River spring/summer Chinook salmon

The Chinook salmon is found along the Pacific coast from the Ventura River in southern California to Point Hope, Alaska. It is also found in northeast Asia, from the Anadyr River south to Hokkaido, Japan.

Juvenile Chinook salmon spend about a year in fresh water before smolting and migrating to the Pacific Ocean. Feeding fish remain in the ocean from three to four years (range, two to eight years) before they mature and return to their parent stream to spawn. The principal spawning months are July through September. Average egg production by a female is 5,000 (range 2,250-7,750). The eggs hatch in about two months, depending on water temperature. The young remain in the gravel two to three weeks after hatching. Juveniles remain in fresh water from a few days to three years. Most juvenile spring Chinook remain in the stream for one year before migrating.

This species may be affected by yew harvest.

Northern Bald Eagle

This eagle is listed as a threatened species in Oregon and Washington. Eagles usually locate nests in the upper canopy of large old growth trees, usually within two or three miles of coastal, lake, or river areas (Stalmaster et al., 1985). Night roosts are generally found in coniferous stands with well-developed canopies.

During winter months, bald eagles forage on water courses that support spawning salmon and/or waterfowl. The eagles generally perch in large deciduous and coniferous trees in close proximity to

feeding areas. Eagles may gather at dusk, collecting in the open branches of large trees. From there they fly to communal night roosts, which are usually located within a few miles of feeding areas.

Bald eagle habitat on the Pacific coast is protected and managed in accordance with "The Pacific Bald Eagle Recovery Plan" (USDI Fish and Wildlife Service, 1986), and the "Working Implementation Plan for Bald Eagle Recovery in Oregon and Washington" (Washington Department of Wildlife, 1989).

This species may roost, nest, and forage in yew habitat.

Northern spotted owl

For more than a decade there has been growing concern and controversy about managing forest lands for the protection of the northern spotted owl. Concern and controversy increased with the June 26, 1990 listing of the northern spotted owl as threatened with extinction under the Endangered Species Act of 1973. Extensive popular and scientific literature is available which discusses various aspects of the controversy.

For a complete discussion of the habitat needs and life history of the northern spotted owl, see:

- "Report of the Advisory Panel on the Spotted Owl" (Dawson et al., 1986);
- "Final Supplement to the Environmental Impact Statement for and Amendment to the Pacific Northwest Regional Guide" (USDA, Forest Service. 1988b);
- The Interagency Scientific Committee's (ISC) "Conservation Strategy for the Northern Spotted Owl" (Thomas et al., 1990);
- The U.S. Fish and Wildlife Service's three status reviews (USDI, 1987; USDI, 1989; Anderson et al., 1990); and
- The June 26, 1990 final ruling that listed the northern spotted owl as a threatened subspecies (Federal Register, 55:26114)

This species forages, roosts, and nests in yew habitat.

Marbled Murrelet

The marbled murrelet, a member of the alcid family, is a robin-sized seabird that congregates to feed primarily in salt water. Murrelets typically feed on small fish and invertebrates within one mile of shore (Marshall, 1988). They are found throughout the North Pacific; the American subspecies is found from Alaska in the summer to wintering grounds as far south as California.

Although marbled murrelets are numbered in the hundreds of thousands in Alaska (Marshall, 1988), and up to 3,000 off the coast of Washington (Spiech et al., in press), the numbers dwindle to approximately 1,000 breeding pairs off the coast of Oregon (Nelson et al., in press), and an estimated 1,650 birds in California (Carter and Erickson, 1988).

Marbled murrelet nests have been found from southeastern Alaska to northern California in a range of forest structures from stands of wholly old growth trees to mixed stands containing mature and old growth trees. Nest sites, characterized by depressions in moss and lichens, have been located on large, lateral branches. Murrelets have been detected as far inland as 43 miles in Washington, 35 miles in Oregon, and 24 miles in California (Nelson, 1990; Paton and Ralph, 1988).

This species may nest in yew habitat.

Grizzly Bear

As omnivorous, opportunistic feeders, grizzly bears use a variety of habitats. Ninety percent of the grizzly bears' diet is vegetation. Areas used by bears in the spring contain early emergent vegetation. Examples of spring bear range include south-facing avalanche chutes and shrub fields. Big game winter range and anadromous fisheries provide concentrated protein sources for bears in the spring and early summer. Summer and fall habitat components are generally composed of grass/forb and shrub communities. Examples of these include avalanche chutes, harvested units, sidehill parks, and open canopy forest. Winter den habitat is often above 6,000 feet in areas of heavy snowpack. Good denning sites may occur near ridges and upper avalanche chutes.

Home ranges as large as 1,004 square miles have been reported (National Wildlife Federation, 1987; Almack, personal communication).

This species may forage in yew habitat.

Valley elderberry longhorn beetle

Information on this species is lacking at this time. It is unknown if this beetle would occur in yew habitat or be affected by yew harvest. Further investigation is ongoing. Species information will be updated as it becomes available.

Endangered Species

Snake River sockeye salmon

Sockeye salmon are native to the Snake River and historically were abundant in several lake systems in Idaho and Oregon. In this century, a variety of factors have led to the demise of all Snake River sockeye salmon except those returning to Redfish Lake in the Stanley Basin of Idaho.

Most of the spawning at Redfish lake is along the lake shore where ground water percolates through the gravel. A single sockeye female may contain as many as 4,000 eggs. The eggs hatch in six to nine weeks, depending on water temperature. The young remain in the gravel for another two to three weeks. During their fresh water life, juvenile sockeye salmon feed largely on zooplankton. The downstream migration of smolts occurs in the spring. The young remain at sea for two to four years before returning as adults.

This species may be affected by the harvest of yew.

Northern Bald Eagle

This eagle is listed as endangered in California, Idaho, and Montana. Eagles usually locate nests in the upper canopy of large old growth trees, usually within two or three miles of coastal, lake, or river areas (Stalmaster et al., 1985). Night roosts are generally found in coniferous stands with well-developed canopies.

During winter months, bald eagles forage on water courses that support spawning salmon and/or waterfowl. The eagles generally perch in large deciduous and coniferous trees in close proximity to feeding areas. Eagles may gather at dusk, collecting in the open branches of large trees. From there they fly to communal night roosts, which are usually located within a few miles of feeding areas.

This species may roost, nest, and forage in yew habitat.

American Peregrine Falcon

Peregrines are limited to areas which contain suitable nesting ledges. Cliffs and bluffs typically found along river courses and other large bodies of water usually provide habitat for nesting peregrines (Call, 1978). Falcons prefer to nest where the concentration of prey, generally smaller birds, is high and where habitat "structural characteristics...may increase prey vulnerability" (Skaggs et al., 1986).

Peregrine habitat on the Pacific coast is managed in accordance with the "Recovery Plan for American Peregrine Falcon" (USDI Fish and Wildlife Service, 1982) and standards and guidelines in the various forest plans.

This species may use yew habitat for foraging and nesting.

Columbian white-tailed deer

This subspecies of white-tailed deer lives in Oregon and Washington, along the Columbia River from Portland to Astoria. It is also found in the Umpqua Valley near Roseburg, Oregon.

Gray Wolf

Gray wolves utilize many habitat types. The availability of prey seems to be the primary factor in determining suitability of habitat. Primary foods for wolves are ungulate species, such as deer, but wolves also consume small mammals such as rodents. There have been reports of home ranges as large as 1,197 square miles (Paradiso and Nowak, 1982).

This species may forage and den in yew habitat.

Woodland caribou

The woodland caribou of North America (Rangifer tarandus caribou) is broken down into two "ecotypes": mountain and northern. These ecotypes are based on the different habitat and behavior patterns of the subspecies. Only the Selkirk population of the mountain caribou is listed under the ESA, and exists in extreme northeastern Washington and northern Idaho, within the Selkirk mountains. This population is shared with British Columbia. Woodland caribou are medium sized members of the deer family (Cervidae), and can be distinguished from other members of the deer family by their large hooves, broad muzzles, and distinctive antlers (both sexes).

Caribou habitat requirements appear to be distinctive, with late winter habitats almost exclusively in the upper subalpine fir timber types with deep snows in excess of 20 feet. Here their diet consists of arboreal lichens of the genus Alectoria and Bryoria (USDI, Selkirk Mountain Recovery Plan, 1985). Spring brings an elevational shift to lower elevation open areas where early greenup of forbs and grasses is the primary diet. As summer approaches the higher elevation, moist Engelmann spruce basins are preferred, and utilized through late summer and rut. Early winter snows move the Selkirk mountain caribou to the lower elevation cedar/hemlock old growth types and the ecotone between the cedar/hemlock-spruce/fir types that provide snow interception during the time when snows are deep but still fluffy. As soon as these deep snows will support the weight of the caribou with their large hooves, they again move to higher elevations and the lichen diet.

This species may forage and winter in yew habitat.

List C

The following are other species of concern that may occur in the yew habitat.

Fish

Bull Trout *(Salvelinus confluentus)*
Steelhead Trout *(Oncorhynchus mykiss)*
Redband Trout *(Oncorhynchus mykiss spp.)*
Oregon Chub *(Oregonichythys crameri)*
Klamath Large-scale Sucker *(Catostomus synderi)*
Pit Sculpin *(Cottus pitensis)*
Slender Sculpin *(Cottus tenuis)*

Birds

Northern Goshawk *(Accipiter gentilis)*
Northern Pygmy-owl *(Glaucidium gnoma)*
Flammulated Owl *(Otus flammeolus)*
Boreal Owl *(Aegolius funereus)*
White-headed Woodpecker *(Picoides albolarvatus)*
Three-toed Woodpecker *(Picoides tridactylus)*
Harlequin Duck *(Histrionicus histrionicus)*
Ferruginous Hawk *(Buteo regalis)*
Upland Sandpiper *(Bartramia longicauda)*
Tricolored Blackbird *(Agelaius tricolor)*
Black Rosy Finch *(Leucosticte arctoa atrata)*

Mammals

Pacific Fisher *(Martes pennanti pacifica)*
Marten *(Martes americana)*
Wolverine *(Gulo gulo)*
Northern Flying Squirrel *(Glaucomys sabrinus)*
River Otter *(Lutra canadensis)*
North American Lynx *(Felis lynx canadensis)*
Preble's Shrew *(Sorex preblei)*
Pacific Western Big-eared Bat *(Plecotus townsendii townsendii)*
White Footed Vole *(Arborimus albipes)*
California Wolverine *(Gulo gulo luteus)*
California Bighorn *(Ovis canadensis californiana)*

Plants

Triangular-lobed Moonwort *(Botrychium ascendens)*
Crenulate Moonwort *(Bortrychium crenulatum)*
Clustered Lady's Slipper *(Cypripedium fasciculatum)*
Constance's Bittercress *(Cardamine constancei)*
Case's Corydalis *(Corydalis caseana spp. hastata)*
Bank Monkeyflower *(Mimulus clivicola)*
Idaho Strawberry *(Waldsteinia idahoensis)*
Deer-fern *(Blechnum spicant)*
Pacific Dogwood *(Cornus nuttallii)*
Leiberg's Tauschia *(Tauschia tenuissima)*
Plumed Clover *(Trifolium plumosum var. amplifolium)*
Soft Rush *(Juncus effusus var. pacificus)*
Hall's Rush *(Juncus halli)*
False Lilly-of-the-valley *(Maianthemum dilatatum)*
Bank Monkey Flower *(Mimulus clivicola)*
Jessica's Aster *(Aster jessicae)*
Piper's Bug-on-a-stick *(Buxbaumia piperi)*
Henderson's Sedge *(Carex hendersonii)*
Short-spored Jelly Lichen *(Collema curtisporum)*
Small Yellow Lady's Slipper
(Cyrpripedium acaulis var. parviflorum)
Henderson's Shooting-star *(Dodecatheon hendersonii)*
Fringed Pinesap *(Pleuricospora fimbriolata)*
(Abronia umbellata spp. breviflora)
(Agoseris elata)
(Agrostis borealis)
(Agrostis howellii)
(Allium bolanderi)
(Allium brandegei)
(Allium dictuon)
(Allium geyeri var. geyeri)
(Allium madidum)
(Allium tolmiei var. platyphyllum)
(Anemone nuttalliana)
(Antennaria aromatica)
(Antennaria corymbossa)
(Antennaria parvifolia)
(Arabis furcata)
(Arabis sparsiflora var. atrorubens)
(Arabis suffrutescens var. horizontalis)

(Arctostaphylos hispidula)
(Arnica viscosa)
(Artemisia campestris spp. borealis var. wormskioldii)
(Artemisia ludoviciana spp. estesii)
(Asarum wagneri)
(Asplenium septentrionale)
(Asplenium viride)
(Aster gormanii)
(Aster sibiricus var. meritus)
(Astragalus arrectus)
(Astragalus arthuri)
(Astragalus diaphanus var. diaphanus)
(Astragalus howellii var. howellii)
(Astragalus microcystis)
(Astragalus peckii)
(Astragalus umbraticus)
(Bensoniella oregona)
(Bolandra oregana)
(Botrychium ascendens)
(Botrychium crenulatum)
(Botrychium lanceolatu,)
(Botrychium lunaria)
(Botrychium minganense)
(Botrychium montanum)
(Botrychium pedumculosum)
(Botrychium pinnatum)
(Botrychium pumicola)
(Botrychium simplex)
(Bupleurum americanum)
(Calamagrostis breweri)
(Calliergon trifarium)
(Calochortus howellii)
(Calochortus longebarbatis var. longebarbatus)
(Calochortus nudus)
(Calochortus umpquaensis)
(Camassia howellii)
(Campanula lasiocarpa)
(Campanula scabrella)
(Cardamine gemmata = [Dentaria gemmata])
(Cardamine pattersonii)
(Carex aenea)

(Carex anthoxanthea)
(Carex atrata var. atrosquama)
(Carex atrata var. erecta)
(Carex buxbaumii)
(Carex circinata)
(Carex comosa)
(Carex concinna)
(Carex densa)
(Carex flava)
(Carex interrupta)
(Carex limnophila)
(Carex macrochaeta)
(Carex horvegica)
(Carex obtusata)
(Carex pauciflora)
(Carex paupercula)
(Carex proposita)
(Carex saxatillis var. major)
(Carex scabriuscula)
(Carex scirpoidea var. scirpoidea)
(Carex scopulorum var. prionophylla)
(Carex stylosa)
(Carex sychnocephala)
(Claytonia lanceolata var. pacifica)
(Collinsia sparsiflora var. bruciae)
(Coptis asplenifolia)
(Corydalis aquae-gelidae)
(Cyperus rivularis)
(Cypripedium fasciculatum)
(Dodecatheon pulchellum var. watsonii)
(Draba aureola)
(Draba cana = [Draba lanceolata])
(Draba longipes)
(Dryas drummondii)
(Dryopteris cristata)
(Epipactic gigantea)
(Erigeron aliceae)
(Erigeron howellii)
(Erigeron oreganus)
(Erythronium elegans)
(Erythronium revolutum)

(Fillipendula occidentalis)
(Frasera umpquaensis)
(Fritillaria campschatcensia)
(Fritillaria glauca)
(Galium kamtschaticum)
(Galium serpenticum spp. warnerense)
(Gentiana douglasiana)
(Gentiana glauca)
(Gentiana newberryi)
(Gentiana plurisetosa = [Gentiana setigera])
(Gentiana setigera = [Gentiana bisetaea])
(Githopsis specularioides)
(Hackelia diffusa var. diffusa)
(Hackelia hispida var. disjuncta)
(Hackelia vensusta)
(Hieracium longiberbe)
(Kobresia simpliciuscula)
(Leptodactylon pungens spp. hazeliae)
(Lewisia columbiana spp. columbiana)
(Lewisia cotyledon var. purdyi)
(Lewisia leana)
(Lewisia oppositifolia)
(Limnanthes gracilis var. gracilis)
(Linanthus bakeri)
(Lobelia dortmanna)
(Loiseleuria procumbens)
(Lomatium englemannii)
(Lomatium erythrocarpum)
(Lomatium greenmanii)
(Lomatium laevigatum)
(Lomatium "pastoralis")
(Lomatium suksdorfii)
(Lomatium watsonii)
(Luzula arcuata)
(Lycopodium annotinum)
(Lycopodium complanatum)
(Lycopodium dendroideum)
(Lycopodium selago)
(Melica stricta)
(Microseris borealis)
(Microseris howellii)

(Microseris laciniata spp. detlingii)
(Monardella purpurea)
(Montia diffusa)
(Muhlenbergia glomerata)
(Navarretia tagetina)
(Ophioglossum vulgatum)
(Orobanche pinorum)
(Oxypolis occidentalis)
(Parnassia kotzebuei)
(Parnassia paulustris var. neogaea)
(Pedicularis howellii)
(Pedicularis rainierensis)
(Pellaea brachyptera)
(Pellaea breweri)
(Pellaea bridgesii)
(Penstemon barrettiae)
(Penstemon glaucinus)
(Penstemon peckii)
(Perideridia erythrorhiza)
(Perideridia howellii)
(Phacelia minutissima)
(Phlox hendersonii)
(Physaria didymocarpa var. didymocarpa)
(Platanthera chorisiana [syn: Habenaria chorisiana])
(Platanthera obtusata [syn: Habenaria obtusata])
(Platanthera sparsiflora [syn: Habenaria sparsiflora])
(Poa grayana)
(Poa laxiflora)
(Poa nervosa var. nervosa)
(Poa piperi)
(Pohlia sphagnicola)
(Polemonium viscosum)
(Polystichum californicum)
(Potentillia nivea)
(Potentillia villosa var. parviflora)
(Primula cusickiana)
(Ranunculus cooleyae)
(Ranunculus oresterus)
(Rhamnus crocea spp. ilicfolia)
(Ribes marshallii)
(Ribes oxyacanthoides spp. cognatum)

(*Ribes oxyacanthoides spp. irriguum*)
(*Romanzoffia thompsonii*)
(*Rorippa columbiae*)
(*Rubus acaulis*)
(*Rubus bartonianus*)
(*Salix candida*)
(*Salix deinortensis*)
(*Salix farriae*)
(*Salix maccalliana*)
(*Salix tracyi*)
(*Salix tweedyi*)
(*Salix vestita var. erecta*)
(*Sanicula marilandica*)
(*Saxifrage adscendens var. oregonensis*)
(*Saxifrage cernua*)
(*Saxifrage debilis*)
(*Saxifrage integrifolia var. apetela*)
(*Scheuchzeria palustris var. americana*)
(*Scribneria bolanderi*)
(*Sedum laxum spp. heckneri*)
(*Sedum oblanceolatum*)
(*Sedum spathulifolium spp. purdyi*)
(*Senecio dimorphophyllus*)
(*Senecio hesperius*)
(*Senecio porteri*)
(*Sidalcea hirtipes*)
(*Sidalcea oregana var. calva*)
(*Silene nuda spp. insectivora*)
(*Silene scaposa var. scaposa*)
(*Silene seelyi*)
(*Sisyrinchium sarmentosum*)
(*Smilax californica*)
(*Sophora leachiana*)
(*Spirea densiflora var. splendens*)
(*Spiranthes romanzoffiana var. porrifolia*)
(*Streptanthus howellii*)
(*Streptopus streptopoides*)
(*Stylocline psilocarphoides*)
(*Sullivantia oregana*)
(*Synthyris pinnatifida var. lanuginosa*)
(*Tauschia howellii*)

(Tauschia stricklandii)
(Thalictrum alpinum var. hebetum)
(Thalictrum dasycarpum)
(Thelypodium brachycarpum)
(Thelypodium eucosmum)
(Tilaea aquatica)
(Trifolium thompsonii)
(Triteleia hendersonii var. leachiae)
(Trollius laxus var. albiflorus)
(Vaccinium myrtiloides)
(Veratum insolitum)
(Viola lanceolata spp. occidentalis)
(Woodwardis fimbriata)

Amphibians and Reptiles
Couer d'Alene Salamander *(Plethodon vandykei idahoensis)*
Wood Frog *(Rana sylvatica)*
Cope's Giant Salamander *(Diamptodon copei)*
Del Norte Salamander *(Plethodon elongatus)*
Larch Mountain Salamander *(Plethodon larselli)*
Siskiyou Mountain Salamander *(Plethodon stormi)*
Red-legged Frog *(Rana auroa)*
Common Kingsnake *(Lampropeltis getulus)*
California Mountain Kingsnake *(Lampropeltis zonata)*

Invertebrates
Wahkeena Falls Flightless Stonefly *(Nemoura wahkeena)*
Beer's False Penny Beetle *(Acneus beeri)*
Burnell's False Penny Beetle *(Acneus bernelli)*
Mt. Hood Primitive Caddisfly *(Eobrachycentrus gelidae)*
Denning's Agapetus *(Agapetus denningi)*
Schuh's Homoplectran Caddisfly *(Homoplectra schuhi)*
Alsea Micro Caddisfly *(Ochrotrichia alsea)*
Fischer's Caddisfly *(Lepidostoma fischeri)*
Cascades Apatanian Caddisfly *(Apatania tavala)*
Blue Mountain Cryptochian *(Crypotchia neosa)*
Green Springs Mt. Caddisfly *(Farula davisi)*
Mt. Hood Farulan *(Farula jewetti)*
Tombstone Prairie Caddisfly *(Farula reaperi)*
Ft. Dick Limnephilus Caddisfly *(Limnephilus atercus)*
Columbia Gorge Caddisfly *(Nepthremma adnersoni)*

Tombstone Prairie Caddisfly *(Oligophlebodes mosthento)*
Haddock's Caddisfly *(Rhyacphila Haddocki)*
One-spot Caddisfly *(Rhyacphila unipunctata)*
Siskiyou Caddisfly *(Tinodes siskiyou)*

Other Common and Scientific Names Used in the Wildlife Sections

Wildlife	Common Name	Scientific Name
Amphibians	Olympic salamanders Tailed frog	*Rhyacotriton olympicus* *Ascaphus truei*
Mammals	Black-tailed deer Deer Elk Moose Mountain beaver Mule deer Racoon Townsend's vole	*Odocoileus hemionus* *Odocoileus spp.* *Cervus elaphus* *Alces alces* *Aplodontia rufa* *Odocoileus hemionus* *Procyon lotor* *Microtus townsendii*
Birds	American goldfinch Hermit thrush Orange-crowned warbler Song sparrow Townsend's solitaire Varied thrush Western bluebird Western meadowlark White-crowned sparrow	*Carduelis tristis* *Catharus guttatus* *Vermivora celata* *Melospiza melodia* *Myadestes townsendi* *Ixoreus naevius* *Sialia mexicana* *Sturnella neglecta* *Zonotrichia leucophrys*
Coniferous Trees	Douglas-fir Grand fir Pacific yew	*Pseudotsuga menziesii* *Abies grandis* *Taxus brevifolia*
Shrubs and Herbs	Umatilla gooseberry	*Ribes oxyacanthoides cognatum*
Ferns	Male fern	*Dryopteris filix-mas*

Environmental Consequences for Animals and Plants

The following provides additional detail and background information on the potential effects of yew harvest on animals and special status plants.

Species Associated With Late-Successional Forests

The yew harvest program would not change the amount of late-successional forest habitat. However, harvesting yew in late-successional forests would change the character of the habitat, and could affect some species. These are poorly understood relationships, and the degree to which this would happen is unknown for most species. In the absence of detailed information on the habitat relationships of species associated with late-successional forests, the effects of yew harvest is assumed to be related to potential effects on animals and other plants. Species for which additional information is available, such as moose, are discussed individually following the general discussion.

Forest Structure and Composition

Alternatives that harvest yew outside of clearcut/shelterwood/seed tree timber sale areas would result in changes in the structure and composition of late-successional forest habitats where the harvest occurs. Yew harvest would affect multilayered forest canopies and plant species diversity, two habitat components that may enhance animal species diversity in late-successional forests. Multilayered stands and stands with higher plant species diversity are considered to be valuable to wildlife because they are believed to support more diverse animal communities. Research has shown that multilayered forest habitats at least sometimes support more diverse bird communities (MacArthur and MacArthur, 1961).

The Interim Guide to the Conservation and Management of Pacific Yew (USDA Forest Service, 1992) assumes that 30 to 50 percent of the midstory could be removed without a significant risk of reducing the abundance and fitness of vertebrates using the area. This is based on findings in a study in the Oregon coast range that removing about 30 percent of the Douglas-fir overstory in half-acre patches did not have appreciable short-term effects on small birds

or mammals (USDA Forest Service, Interim Guide, 1992). In areas where dense patches of yew make up a higher proportion of the midstory layer, effects on animal and other plant populations and communities may be greater than in areas where other plant species contribute more to the midstory vegetation.

Other habitat components of late-successional forests include large trees, snags and logs. These would be less affected by yew harvest. The large tree component would not be affected by yew harvest since the Pacific yew is a smaller understory tree species where it occurs in late-successional forests.

Yew snags would not generally be directly affected by harvest in late-successional forests. At this time, yew harvest focuses on live or recently dead yew trees and shrubs. However, the harvest of live trees would reduce the number of snags that might be available in the future. A very small proportion of all snags are Pacific yew. Species using snag habitat that is not related to a particular species of tree would not be significantly affected by yew harvest. There are no species currently known to depend on yew snags. The effects of the alternatives on such species, if they exist, are unknown. Most of the wildlife-snag relationships that have been identified indicate that larger diameter and taller snags have a greater value for cavity users. Since yew snags tend to be relatively short, with relatively small diameters, it is assumed that their value to cavity users is low.

Yew logs are relatively small and scarce in most areas, compared to those of other species, but their extremely slow rate of decay makes them rather unique. Yew harvest could result in additional yew wood being left in non-timber sale areas. These additional logs would be unlike naturally occurring logs in that they would be peeled, cut into pieces and, possibly, piled. The effects of these changes to wildlife are unknown, but the abundance of some species may increase with increasing numbers of yew logs. Where yew is abundant, large quantities of logs and branches left on the ground could impede movements of some species. The role of yew logs in streams and riparian areas is discussed below (and in the water quality section).

Moose and Other Ungulates

Yew harvest in old growth grand fir/Pacific yew forests on moose winter range in northern Idaho would affect forage quantity and forage availability as a result of snow interception and thermal cover. Yew harvest would result in an increase in forage two years after harvest, but this would not be available to moose if the combined canopy coverage of the overstory grand fir and understory yew was not great enough to intercept the snow. The loss of thermal cover could put additional stress on moose during severe winter weather.

Although yew is a preferred browse species and, at times, provides thermal and hiding cover, deer and elk are opportunistic in their feeding habits and do not depend heavily on yew in most areas. There may be site-specific situations where yew is particularly important to local deer or elk populations for food or cover.

High open road densities have significant effects on ungulates due to disturbance by traffic, reduction in habitat availability adjacent to roads, and increased vulnerability of animals to legal and illegal harvest. If additional road building or opening of currently closed roads occurs in connection with yew harvest and leads to higher open road densities, deer, elk and moose would be subject to greater stress, their distribution could become more restricted, and their abundance could decline. If yew harvest occurs in fawning or calving areas, disturbance could result in increased fawn and calf mortality rates. In areas with abundant yew, material left after harvest could interfere with animal movements.

Other Species

Note: An in-depth discussion of the effects of yew harvest on spotted owls is included at the end of this section.

It is assumed that yew fruit is important to fruit-eating rodents and birds only sporadically over space and time because fruit production is patchy over the landscape (USDA, 1992) and fruit-eating species are not limited to areas with yew. In areas where yew is abundant, removal of large amounts of yew could affect these species. Although yew harvest probably would not eliminate

fruit-eating species from an area, population numbers or the survival of offspring could be reduced in areas where fruit is abundant. In turn, this could affect other species that prey on the fruit eaters.

Cumulative Effects

There are significant risks, in terms of effects on wildlife and other plants, associated with a program which would harvest yew all across the landscape in only a few years (e.g. the four-five years projected in this EIS). The knowledge that we currently have about the relationships of Pacific yew to other species is extremely limited. For example, the descriptions of what constitutes good quality winter range for moose on the Nez Perce National Forest in northern Idaho are from very limited study, and more research has been done on moose/yew relationships than for any other species or group of species.

If yew is harvested at the specified harvest levels on all of the available acres, the effects on wildlife diversity may be substantially greater than if only a portion of the acres are harvested. Options for selecting harvest areas would be limited if harvesting was done on all acres available under existing forest plans or BLM resource management plans. For example, harvest in an area where yew makes up a greater proportion of the midstory vegetation probably has greater effects than harvest in an area where other tree species provide a significant proportion of that layer. Harvest at the prescribed level over all acres that meet the minimum requirements could result in the removal of some habitat features from the landscape. For example, if all thick clumps of yew were thinned or removed, animals that depend on thick clumps would be significantly affected on a broad landscape scale. These aspects of wildlife ecology are complex, difficult to study, and poorly understood.

An intensive program to harvest yew over large areas in the short time frame of a few years would have significant effects on ungulates and other species sensitive to human disturbance. Increased traffic and increased densities of open roads could substantially reduce effective ungulate habitat in some areas.

Many roads would probably have to be opened to accommodate yew harvesters and use of those roads by yew harvesters and others would increase. A substantial increase in people working throughout the forest would also disturb ungulates and other wildlife species. Since much of the yew harvest season overlaps with calving and fawning seasons, increased human activity in calving and fawning areas would cause disturbance at a sensitive time of year. These stresses could result in poor animal condition and increased mortality. Other species that avoid human contact could be similarly affected.

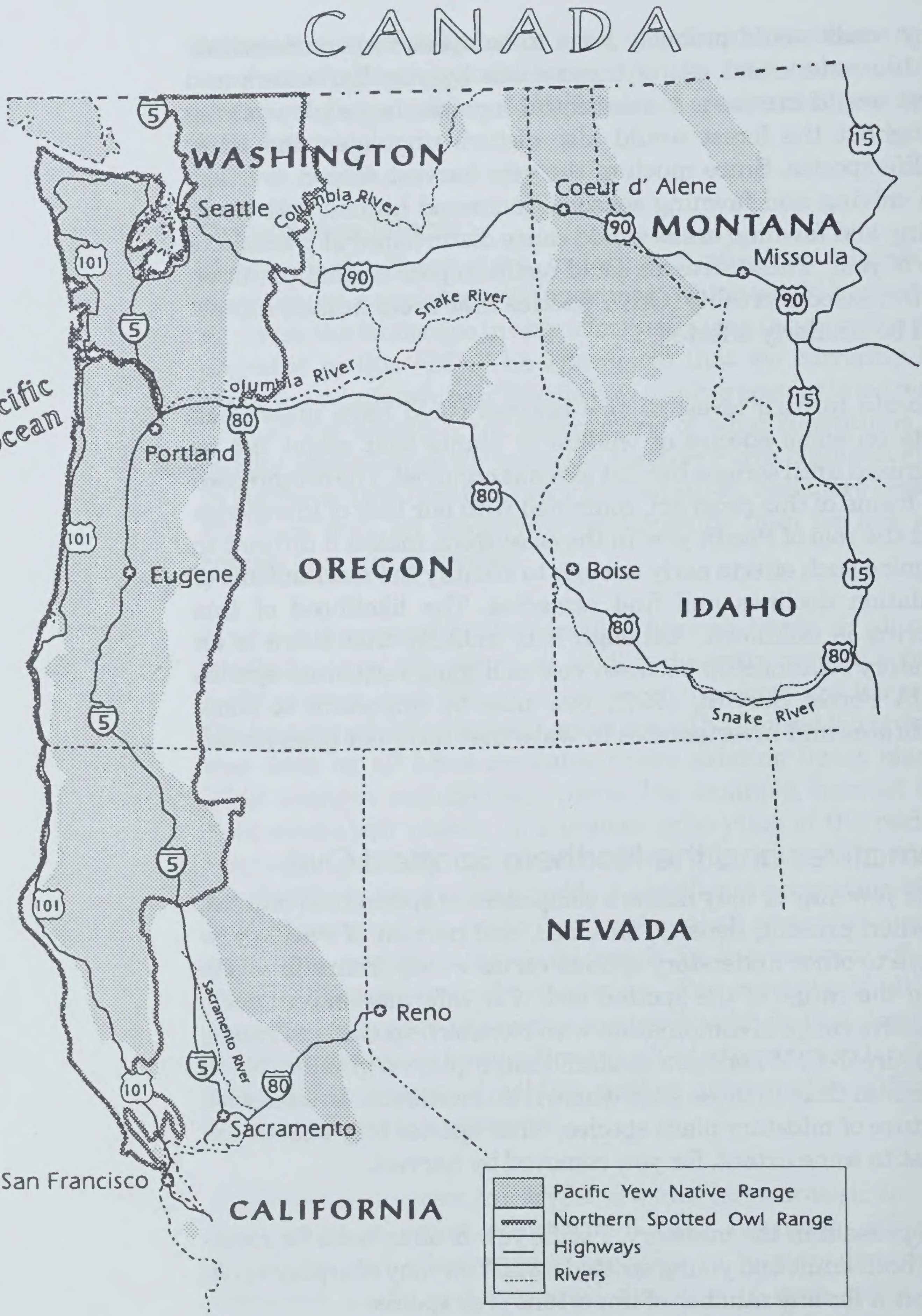
Moderate to high levels of yew harvest could have unforeseen effects on some species of wildlife or plants that might not be recognized until serious habitat loss has occurred. The compressed time frame of this program, combined with our lack of knowledge about the role of Pacific yew in the ecosystem, makes it difficult to recognize such effects early enough to identify the mechanisms of population declines and find remedies. The likelihood of this occurring is unknown. Although it is unlikely that there is an obligatory relationship between yew and <u>most</u> vertebrate species (USDA Forest Service, 1992), yew may be important to some vertebrates and invertebrates in ways that have not been identified.

Alternatives and the Northern Spotted Owl

Pacific yew may or may not be a component of spotted owl habitat, and when present, density, size, age, and percent of Pacific yew relative to other understory species varies widely from site to site within the range of the spotted owl. (For information on Pacific yew native range in combination with Northern spotted owl range, see Figure J-1.) Where yew is abundant, it plays a greater role in owl habitat than in those sites where it is uncommon. In sites with a mixture of midstory plant species, other species may substitute, at least to some extent, for yew removed by harvest.

When present in the midstory, Pacific yew is often used for roosting by both adult and young spotted owls. Yew may also play a role as habitat for any number of important prey species.

Figure J-1: Pacific Yew Native Range and Northern Spotted Owl Range



Although there is an absence of data, it is generally felt that some proportion of a stand can be removed without causing significant habitat changes for vertebrate species. Conversely, if a large percentage of the stand is removed, especially in areas where yew is abundant, the stand structure may be changed enough to cause a reduction in or loss of vertebrate species (USDA Forest Service, Interim Guide, 1992). Spotted owl habitat would probably not be impacted by the harvest of needles, provided the tree is not killed.

Effect on Prey Species

Pacific yew is closely associated with late successional stage forests and riparian situations throughout its range. A large number of animal species, some of which are prey species for owls, are also associated with these same late successional stage and riparian situations. The northern flying squirrel, bushy-tailed wood rat, red tree vole, and red-backed vole are examples of prey species associated with these sites.

No studies currently are available that describe the relationship between prey species and Pacific yew. It is known, however, that yew of varying height and age helps to create a multi-layered forest that provides perches, dispersal opportunities and travel routes for arboreal mammals. Carey et al. (1991) reports that some arboreal mammals, such as the red tree vole, move almost exclusively through the canopy and are reliant on a closed and layered canopy for food sources, feeding cover, predation cover, and dispersal or other movement.

Alternatives

Alternatives A and B have the least impact because they propose little (Alt. B) or no (Alt. A) habitat disturbance in addition to that normally occurring from implementing forest or resource management plans. Alternative B does remove yew, but only after (or shortly before) the overstory has been removed by timber harvest. The greatest impact occurs with the removal of the overstory. Alternatives C through G2 require regeneration of yew following harvest, and have fewer long-term impacts.

Alternatives C, D, and F provide for harvesting yew from non-sale areas and thinning units, as well as from timber harvest areas. These alternatives have a greater potential to impact spotted owl prey habitat because they permit harvest in extensive areas of currently suitable owl habitat. Forest plans and BLM resource management plans provide that many of these non-sale areas will be scheduled for timber harvest at some point in the future. Alternatives C, D, and F, however, will accelerate the impact on understory vegetation by removing a portion of yew before the scheduled timber harvest. Impacts increase with the percentage of yew removed. The impacts of Alternative G1 would be similar to those of Alternative D but more total acres would be involved because of reduced leave tree requirements.

Alternative G2, in addition to providing yew harvest from sale areas and non-sale areas, provides for harvest from Owl Conservation Areas (OCAs) and has the greatest potential for impacting spotted owl prey habitat because the largest area is available for harvest.

In addition, harvest within Owl Conservation Areas conflicts with direction stated in the "Final Environmental Impact Statement for the Management of the Northern Spotted Owl in the National Forests," and in "A Conservation Strategy for the Northern Spotted Owl." The goal for Owl Conservation Areas is to "maintain, over the forest landscape, a population of northern spotted owl that has a high probability of continued existence throughout its range."

Effect on Roosting Habitat

During the warm summer months, northern spotted owl roost sites are usually cool shady sites located near streams on the lower one-third of slopes. Owls tend to roost low in the forest understory in small trees and shrubs (Forsman, 1976; Solis, 1983). Spotted owls respond to variations in temperature and exposure by moving within the canopy to find favorable conditions (Forsman 1976; Barrows and Barrows, 1978; Forsman, 1980; Barrows, 1981; Solis, 1983; Forsman et al., 1984). By roosting in the shade of the understory during the warm weather, owls reduce their exposure

to high temperatures and solar radiation (Forsman, 1976; Barrows and Barrows, 1978) and may reduce the metabolic energy required for thermoregulation (Forsman, 1980).

Pacific yew commonly serves as a roost site, and facilitates movement through the understory. No information currently is available concerning the size, amount, and distribution of Pacific yew occurring in summer roost areas. The effects of yew removal have not been evaluated through formal study.

Intuitively, the greatest effect can be expected in summer roost areas where yew is the dominant understory species and where a large percentage of the large size class (>1 11" DBH) of trees are removed. Minor impacts can be expected where summer roosting does not occur or where understory vegetation is abundant and varied and when smaller (<1 10" DBH) yews are harvested.

Alternatives A and B would have no effect on roosting habitat. Alternative A does not harvest yew and Alternative B harvests from timber sale units. Sale units are not suitable habitat following the harvest of the overstory stand.

Alternatives C, D, and F allow yew harvest in non-sale areas. These alternatives have a greater potential to reduce the quality of roosting habitat in areas of suitable habitat outside of OCAs. Many of the current non-sale areas will be scheduled for timber harvest in the future, but these alternatives will allow removal of part of the multistoried stands in the interim before final harvest. The impacts of Alternative G1 would be similar, but somewhat greater than Alternative D because the reduced leave tree requirements will increase the total acres where yew harvest can occur. Impacts increase with the percentage of yew harvested and where Pacific yew is the dominant understory species.

In addition to providing yew harvest in sale areas and selected non-sale areas, Alternative G2 allows yew to be removed from Owl Conservation Areas, and because of this, has the greatest potential of impacting roosting habitat of any of the alternatives. Loss of habitat or habitat quality in the Owl Conservation Areas may have long-term effects and could reduce the productivity of some OCAs.

In addition, harvest within OCAs conflicts with the direction prescribed in "A Conservation Strategy for the Northern Spotted Owl" and the "EIS for Management of the Spotted Owl in the National Forests." The conservation strategy states in part, "Activities within OCAs should be consistent with their primary management prescription to ensure that owls in OCAs have high probability of persistence (details in appendices O and Q). In particular, forests in OCAs should be maintained in superior habitat condition for owls, and younger forest and logged sites should be allowed to mature into superior habitat."

Biological Assessment

- Biological Assessment will be included in the Final Pacific Yew Environmental Impact Statement document.

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Appendix K

Taxol

Appendix K

Taxol

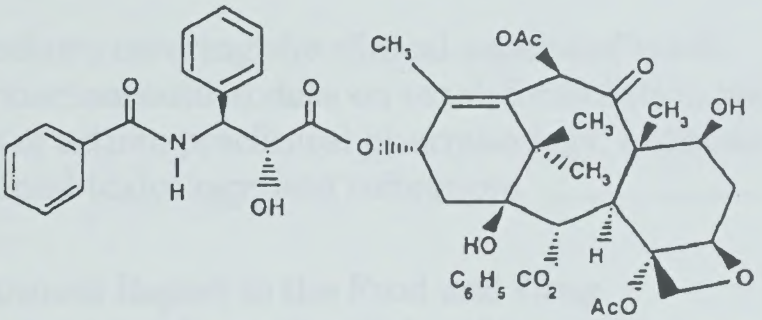

Table of Contents

The following is a chronology of the development of taxol as a cancer-fighting drug:

1963: NCI found that yew samples showed activity against 9KB cancer-cell tissue culture. NCI sent a subsample to Monroe Wall, Ph.D., a medicinal chemist working under contract to NCI at Research Triangle Institute in North Carolina.

1964: Wall's group found that a crude extract of the yew bark was effective in both the cancer-cell tissue system and against a mouse leukemia. They worked to isolate the primary active principle of taxol.

1966: Wall asked NCI to give the yew material special priority for research. He isolated the active principle and named it taxol.

1969: NCI checked the activity of all parts of Pacific yew. They now knew three things— the structure of taxol, its success in cancer screens, and something about how it worked against cancer.

1971: Wall, with Mansukh Wani (at Research Triangle Institute) and Andrew McPhail (of Duke University), published the structure of the taxol molecule, a complex diterpene with an unusual oxetane ring and an ester side chain.

1974: Taxol began to show results against a recently developed B16 mouse melanoma system. During the 1970s, cytotoxicity tests continued with tumor lines in new animal screens, including human tumor xenografts (tissues grafted from one species to another).

1977: Preclinical work on taxol began. NCI contacted Susan Horowitz (professor of molecular pharmacology at Albert Einstein College of Medicine in the Bronx), working under an NCI Cancer Research Emphasis Grant, to ask her to investigate how taxol worked on cancer cells. With graduate student Peter Schiff, she found that taxol inhibited the replication of human tumor cells. (Specifically, taxol induces "tubulin polymerization" and inhibits disassembly of microtubules, an activity necessary to complete cell division.)

1978: Taxol showed positive results in human cancer xenografts. Taxol showed activity in three systems, including a human breast cancer xenograft developed in the late 1970s.

1979: Horowitz and Schiff published their findings about taxol's action of freezing microtubules and causing the cell to die.

1980: Toxicology studies began. Scientists looked for a suitable surfactant formulation for administering the insoluble drug.

1982: NCI approved taxol for filing an Investigational New Drug Application (INDA) with the Federal Drug Administration.

1983: Phase I clinical trials began, testing patients who were not responding to other treatments, determining doses and toxicity, and generating data on dose limits of taxol.

1987: NCI contracted for collection of 60,000 (Daly, 1992) pounds of dry Pacific yew bark.

1988: Phase II clinical trials showed 30 percent improvement in patients with unresponsive cases of advanced ovarian cancer.

1989: Trials of taxol progressed for other forms of cancers: breast, cervical, colon, gastric, non-small-cell lung, prostate, head and neck, small-cell lung, and renal. NCI contracted for an additional 60,000 pounds of dry bark.

1990: Phase II trials showed 48 percent tumor shrinkage with metastatic breast cancer patients who had at least one prior chemotherapy regime. (Metastatic refers to cancers which tend to spread from one body part to another.)

1992: Clinical trials were conducted at 20 centers on a number of different cancers, with some experimenting with combinations of chemotherapies.

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Taxol and Related Anticancer Drugs

Taxol is a plant-derived anticancer drug currently being evaluated in clinical trials supported by the National Cancer Institute (NCI). It was first isolated from the bark of the Pacific yew tree, *Taxus brevifolia*, which is native to old-growth forests of the Pacific Northwest, but it is also found in bark and needles of related species throughout the world.

Development of taxol has been slow because a large amount of bark (the equivalent of three or more trees) is needed to treat a single patient. Also, the concentration of taxol in Pacific yew bark--still the only acceptable source for trials in humans--is low, making it expensive to extract, and it is not soluble in water, complicating its use in patients.

Clinical Trials

Scientists first began clinical studies of taxol in 1983, and by 1988 preliminary results suggested that it was active against ovarian cancer. More definitive trials since that time have continued to be encouraging.

Taxol has been tested in more than 200 patients with recurrent ovarian cancer, which is generally resistant to chemotherapy. The tumors of at least 30 percent of these patients have responded to a significant degree, with some responses lasting more than a year. Early

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studies indicate that taxol could also play an important role in treating several other types of cancer, including advanced breast cancer.

Like other cancer drugs, taxol has unpleasant side effects and occasional severe toxicity, but these adverse effects are generally acceptable relative to the drug's benefits.

Unique Mode of Action

Taxol has been the focus of great scientific interest because of its unique mode of action as well as because of its potential for treating cancer.

Cells have fibrous skeletons composed of structures known as microtubules that assemble and come apart as the cells progress through their life cycles. Interference with microtubule assembly and disassembly blocks cell division.

Certain anticancer drugs act by inhibiting microtubule assembly. Taxol, in contrast, interferes with cell function and division by promoting assembly and inhibiting disassembly of microtubules, causing the cells to become crowded with bundles of the thread-like structures. Because its mode of action differs from that of other anticancer agents, scientists hope taxol may prove effective in treating cancers that have grown resistant to other drugs.

Increasing Demand

The encouraging results from taxol clinical trials have increased demand for the drug, both from researchers wanting to perform additional trials and from patients who have few alternative options and would like to take taxol either within or outside of trials.

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3

This year, NCI officials expect more than 4,000 patients with breast, ovarian, and several other types of cancer to receive taxol in trials, and about 2,000 patients with ovarian cancer to receive the drug on a compassionate basis. However, the potential demand could be much greater, especially if, as anticipated, taxol soon receives approval from the Food and Drug Administration (FDA) to be marketed for use in refractory (treatment-resistant) ovarian cancer.

To meet the demand for taxol and facilitate eventual marketing, NCI needed to work with a company that could produce the drug in quantity. In January 1991, after an open competition, the institute signed a Cooperative Research and Development Agreement (CRADA) with the pharmaceutical manufacturer Bristol-Myers Squibb (BMS). Under the terms of the CRADA, BMS received exclusive access to data from NCI's preclinical studies and clinical trials of taxol. In exchange, the company agreed to supply NCI with the drug for trials and compassionate use, to pursue a New Drug Application with the FDA for permission to market taxol, and to seek alternative sources of the drug.

In order to carry out its obligations under the CRADA, BMS has been working with the Department of Agriculture's Forest Service and the Department of the Interior's Bureau of Land Management in a concerted effort to collect large amounts of Pacific yew bark.

During the 1991 fiscal year, BMS organized the collection of over 825,000 pounds of yew bark from national forest lands in Oregon, Washington, Idaho, and Montana. Taxol extracted from the bark is being delivered to NCI by BMS and will be used in clinical trials.

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However, the Pacific yew is a limited resource located in old-growth forests that serve as a habitat for the endangered spotted owl. For this reason, and because bark collection and taxol extraction are difficult and expensive, NCI and BMS do not consider yew bark to be a viable source of taxol over the long term. NCI has thus been encouraging research directed toward finding alternative and renewable sources of taxol.

Varied Approaches

Researchers engaged in this effort have been exploring a variety of approaches, including extraction of taxol from yew needles (a renewable resource), genetic manipulation of plants to increase the yield of taxol, propagation of trees, semisynthesis, total chemical synthesis, and plant tissue culture.

NCI has been supporting several of these approaches for some years. The level of support amounted to $1.5 million at the beginning the 1991 fiscal year. In July 1990, the institute issued a Request for Applications for new research grants in this area, and additional grants of $2.28 million have since been awarded, bringing total current funding to $3.78 million. NCI has also expressed willingness to collaborate with pharmaceutical companies to obtain taxol analogues (related compounds) from sources other than bark.

NCI officials expect that within two to three years sufficient taxol will be available from alternative sources to reduce the pressure for bark collection. However, it may be as long as five years before the need for bark is completely eliminated.

5

Synthesis and Semisynthesis

A number of outstanding chemists have been trying to synthesize taxol, and they have made significant progress. At Stanford University, a researcher supported by NCI and BMS has succeeded in duplicating most of the complex structure that lies at the core of the taxol molecule. He and his colleagues hope to be able to produce the entire molecule by the end of 1992.

Much work will be required before this bench-level synthesis can be scaled up enough to make a significant contribution to taxol supply, and it is not clear whether total chemical synthesis will ever be a practical means of producing the drug for clinical use. However, this approach does offer opportunities for scientists to synthesize structural analogues of taxol for research studies and, potentially, for clinical development.

Partial synthesis of taxol, starting with a complex natural product, is more likely to be commercially feasible. Working along these lines, a chemist at Florida State University in Tallahassee has developed an improved method of semisynthesis, starting with baccatin III, a taxol precursor found in needles of several yew species. This process has been licensed to BMS, which expects to use the method to produce large quantities of taxol within the next year or two.

Alternative Sources

Meanwhile, researchers at a Forest Service laboratory in Madison, Wis., have been studying methods of extracting taxol from heartwood of the Pacific yew. This approach

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6

could increase the total yield of taxol from each tree. However, it would still require destruction of trees.

Several different *Taxus* species might eventually be used to furnish taxol. The compound has been identified in bark and leaves of trees native to India and Europe as well as North America. Plants of the yew family currently being grown in commercial nurseries constitute another potentially important, and renewable, source of taxol.

With support from the NCI and the Department of Agriculture (USDA), and with the help of the University of Mississippi and Ohio State University, the Zelenka Nursery in Grand Haven, Mich., has coordinated the collection of large amounts of needles from ornamental yew plants and has found that this material contains significant amounts of taxol.

Ornamental yew are grown in nurseries for several years before they are sold, and they are trimmed every year. Because these cuttings, which have been treated as waste until now, are readily available, they are a potentially useful source of taxol.

BMS is working with the University of Mississippi on a related project and is helping to fund construction of a pilot natural products production facility to aid in the research.

Building on the concept of obtaining taxol from cultivated plants, BMS and the Weyerhaeuser lumber company have agreed to cooperate to produce taxol from genetically selected stocks. The goal of the project is to grow large numbers of plants with a high yield of taxol. Weyerhaeuser has agreed to supply BMS with taxol-containing plant material through the end of the decade. Since signing the agreement with BMS, Weyerhaeuser has planted more than four million *Taxus* seedlings as starters for future production populations.

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Biosynthesis

Although some experts believe that biosynthesis of taxol by plant tissue is likely to take longer than other approaches to become a practical source of the drug, a number of researchers and companies have been exploring this option. A USDA plant physiologist and her co-workers, for example, have developed and patented a technique for growing cells of yew plants in bioreactors (tissue culture vessels), where they produce taxol and taxol analogues.

Phyton Catalytic, Inc., a plant biotechnology company in Ithaca, N.Y., has an exclusive license from USDA to produce taxol in tissue culture using USDA's method, and they have already done this on a small scale. The company has been working in collaboration with BMS to optimize the process and expects to be able to produce taxol commercially within the next few years.

Working independently, ESCAgenetics Corp. of San Carlos, Calif., announced last June that it, too, had succeeded in producing taxol in plant cell culture.

Taxotere

At present, one of the most promising alternatives to taxol is Taxotere, a related compound, or analogue, developed by the French pharmaceutical company Rhône-Poulenc. The company's U.S.-based spin-off, Rhône-Poulenc Rorer (RPR), has patents on the drug and permission from the FDA to conduct clinical trials of the agent in humans.

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Taxotere is produced by chemically altering a compound extracted from needles of the European yew. These needles are abundant, easily collected, and renewable, and the yield of Taxotere from needles is greater than that of taxol from yew bark.

The structures of Taxotere and taxol are similar, and the two drugs have similar effects on human cells in culture. Taxotere, like taxol, interferes with disassembly of microtubules, thereby blocking cell division. However, Taxotere is somewhat more water-soluble than taxol, which could be an advantage in formulating and administering the drug.

Taxotere has shown promise in early clinical trials, and NCI has been eager to work with RPR to test the new drug in additional trials. To this end, the two parties have recently signed a CRADA for clinical development of Taxotere.

Under the agreement, NCI and RPR will cooperate in conducting clinical trials of Taxotere in a number of cancers, including ovarian cancer, adult acute leukemia, and pediatric leukemias and solid tumors. Plans call for the new agent to be tested both as a single agent and in combination with other drugs. RPR also will conduct independent studies of Taxotere in several cancers.

Deletion Analogues and Prodrugs

Both taxol and Taxotere are complex molecules. Scientists would like to find a simpler variant with similar activity that could be easily synthesized in the laboratory. As part of this effort, a number of chemists have been studying "deletion analogues" of taxol--variants of the molecule with small portions missing--to determine which parts of the structure are essential for taxol's antitumor effect.

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Meanwhile, researchers at Virginia Polytechnic Institute in Blacksburg, Va., are focusing on developing water-soluble taxol prodrugs--inactive compounds that could be delivered to the patient more easily than taxol and that would be converted into taxol or related active drugs within the body.

The need to fill the taxol supply gap has generated intense effort on the part of NCI, other government agencies, and researchers and businesses in several countries. This effort appears to have paid off, and taxol, possibly along with related compounds, should become widely available for use in cancer patients within the next few years.

# # #

Bristol-Myers Squibb Company

News

THE SEARCH FOR ALTERNATIVE SOURCES OF TAXOL

BACKGROUND INFORMATION

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According to the National Cancer Institute (NCI), taxol is one of the most important anti-cancer drugs discovered in the past decade. The drug, a natural compound derived from the bark of the Pacific yew tree, has shown promise in treating patients with refractory ovarian cancer, a disease which kills nearly 12,500 women each year. Yew bark is the only source of the drug approved for use in humans at the current time.

To expedite the development of taxol so that this promising drug is widely available to cancer patients, NCI signed a Cooperative Research and Development Agreement (CRADA) with Bristol-Myers Squibb Company in January, 1991, after a competitive process involving several pharmaceutical companies. The agreement requires Bristol-Myers Squibb to supply taxol to the NCI for clinical research and to file a New Drug Application for taxol as quickly as possible. Although NCI is still conducting clinical testing on several tumor types, Bristol-Myers Squibb expects to file a taxol new drug application seeking approval to market taxol for refractory ovarian cancer sometime in 1992.

At the same time, Bristol-Myers Squibb Company is aggressively pursuing alternative methods of producing taxol to decrease its dependence on Pacific yew bark. The company recognizes that the Pacific yew tree is a precious and finite resource, and does not consider it a viable source for long-term production of taxol.

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To find alternative sources of the drug, the company is conducting research in its own laboratories and supporting multiple research programs around the world. Already many advances have been made in finding ways to relieve the reliance on yew bark. Bristol-Myers Squibb firmly believes it will not be necessary to make a choice between the future of the Pacific yew and human lives because of its aggressive efforts in pursuing simultaneous searches for alternative sources. Within two years, sources other than bark will begin to be utilized for taxol production on a commercial scale; within three years, reliance on bark will decrease substantially; and within five years, the need for bark should cease completely.

ALTERNATIVE SOURCES AGREEMENTS

As of March, 1992, Bristol-Myers Squibb has entered into over a dozen agreements with various companies, researchers and academic institutions, and has committed millions of dollars to the research and development of alternative sources of taxol. It also continues to negotiate with other companies and universities on collaborative efforts to find alternative sources.

Some of the most promising research programs include:

Extracting taxol from renewable sources, such as twigs and needles of various Taxus species. Called biomass, these sources can be collected without damaging the plant;

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Semi-synthesis, which chemically converts a natural material similar to taxol -- for example, baccatin III found in biomass -- into taxol;

Plant cell culture, in which taxol would be produced in the laboratory from cells of yew tissues, including roots and leaves; and

Total synthesis, which chemically duplicates the taxol molecule. Researchers attempting to produce a synthetic taxol thus far have been unable to duplicate the entire taxol molecule because of its complexity.

RESEARCH PROGRAMS

Following are specific programs supported by Bristol-Myers Squibb in its comprehensive search for alternative sources.

I. CULTIVATED YEW BIOMASS

Taxol has been found in other *Taxus* species around the world. However, varying amounts of taxol found in these plants and the difficulties associated with handling and storing the biomass may make them more impractical to harvest than yew bark. One strategy to address these problems is commercial yew plantations.

Weyerhaeuser Company

Bristol-Myers Squibb signed a three-year research agreement with Weyerhaeuser Company in August, 1991, to investigate the large-scale cultivation of varieties of Taxus to help meet the need for taxol. A second agreement between the companies provides for Weyerhaeuser to supply Bristol-Myers Squibb with biomass material containing taxol through the end of the decade.

Weyerhaeuser annually grows about 280 million yew seedlings in its nurseries and has been involved in yew and related taxol research for more than four years. The goal of the program is to grow large numbers of promising taxol-containing yew trees over the next decade.

Weyerhaeuser has planted more than four million Taxus seedlings since the agreement with Bristol-Myers Squibb was signed, and currently has over 20,000 yew trees in research trials. Once the seedlings have rooted, they will be planted in the ground and allowed to grow. As early as late 1994, the trees will be harvested and used for biomass to support taxol production. During 1992, Weyerhaeuser expects to plant five million rooted cuttings at several western nurseries.

University of Mississippi

Bristol-Myers Squibb has signed a $2.45 million research and development agreement with the University of Mississippi to investigate using raw materials from ornamental shrubs as an alternative source for taxol.

Scientists at the University's Research Institute of Pharmaceutical Sciences have devised a strategy for extracting taxol out of needles clipped from ornamental yews during the normal pruning process. The grant from Bristol-Myers Squibb will enable the research team to refine its process and work toward producing large quantities of taxol economically.

Bristol-Myers Squibb also is providing the University of Mississippi with $500,000 toward construction of a pilot natural products production facility to aid in the research.

II. SEMI-SYNTHESIS

Florida State University

Researchers are aggressively trying to build a synthetic taxol molecule which would lessen the burden on the Pacific yew tree because it allows taxol to be produced from related compounds in other plants. Through a five-year, $1.4 million grant, Bristol-Myers Squibb is supporting research at Florida State University to synthesize taxol chemically.

ALTERNATIVE SOURCES-Pages 6

Florida State already has licensed a semi-synthetic process. Researchers have focused on piecing together the highly complex taxol molecule in the laboratory. The taxol molecule has two parts; the main, which has not been duplicated, and a side chain that has been synthesized. An efficient laboratory-scale method has been devised for attaching the side chain to the main part of the molecule. The main part is a naturally-occuring taxol precursor, which can be isolated from the needles of some yew species. The process is being perfected in the laboratory and must be scaled up before wide-scale production is possible.

Bristol-Myers Squibb is also in the final stages of negotiations with a company with a history of extracting compounds from natural products. Under the agreement, the company would collect renewable biomass from species of <u>Taxus</u> in Europe and Asia and extract 10-deacetyl-baccatin III. Through the semi-synthetic process licensed from Florida State University, the material would be converted into taxol. Deliveries would begin in 1992; Bristol-Myers Squibb expects to produce large quantities of taxol through this method within a few years.

III. PLANT CELL CULTURE

<u>Phyton Catalytic, Inc.</u>

Bristol-Myers Squibb has established a collaborative research and development partnership with Phyton Catalytic, Inc., to develop a plant cell tissue culture process for the production of taxol.

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Phyton Catalytic, an Ithaca, N.Y., plant biotechnology company, was the first commercial organization to produce taxol in a tissue culture system. It has an exclusive license from the U.S. Department of Agriculture to produce taxol in a tissue culture system. Although substantial progress has been made with this approach, it will take several years to scale up the process and produce large amounts of taxol.

Bristol-Myers Squibb is also working with Hauser Chemical Research on developing and scaling up the process for commercializing many of the above alternative sources.

IV. TOTAL SYNTHESIS

Ohio State and Stanford Universities

The complexity of taxol's chemical structure has prevented researchers from totally synthesizing the drug. Bristol-Myers Squibb is supporting research efforts at Ohio State University and Stanford University to find economical ways to synthesize taxol.

A professor of chemistry at Ohio State embarked on a two-year, $360,000 research program in August, 1991. He and his research team are attempting to assemble the framework of the taxol molecule to create synthetic taxol. Although initial progress has been promising, the final stages of the project are still not imminent. Once total synthesis is accomplished in a laboratory, the next question is whether it could be scaled-up to produce large quantities of taxol.

- more -

Analogs, Prodrugs, etc.

In addition to alternative sources research, Bristol-Myers Squibb is working to improve the taxol drug and search for better taxol derivatives. Bristol-Myers Squibb is funding efforts into chemical research involving taxol at the University of Kansas where researchers are studying water soluble derivatives of taxol, and at Virginia Polytechnics Institute. At Virginia Tech, researchers are investigating several compounds similar to taxol that could be used in future development of the drug. The work is being partially supported by a $260,600 grant over three years from Bristol-Myers Squibb.

Researchers are attempting to prepare water-soluble, chemical derivatives of taxol also known as prodrugs, which would have the same capabilities of the parent drug and improved physical properties. Once introduced in the body, the prodrug would convert back into taxol. This process can circumvent problems due to taxol's insolubility.

Virginia Tech also is working on a process to convert Cephalomannine, a compound similar to taxol, into taxol. Cephalomannine also is found in the yew bark. The process would allow more of the natural material now harvested to be used in taxol production.

Related research for the NCI includes investigating how taxol interacts with cells to gain a better understanding of its cancer-fighting qualities, and creating taxol analogs, compounds that are chemically related but with a small variation from the parent drug.

# # #

CLINICAL BROCHURE

TAXOL

IND 22850

NSC 125973

Revised July 1991

Drug Sponsor:

Division of Cancer Treatment
National Cancer Institute
Bethesda, Maryland

This document contains both published and unpublished data describing the results of preclinical trials sponsored by the Division of Cancer Treatment, NCI, with this agent. The unpublished data are preliminary and should not be quoted or used for any purpose other than as guidance in developing clinical trials.

TABLE OF CONTENTS

SUMMARY

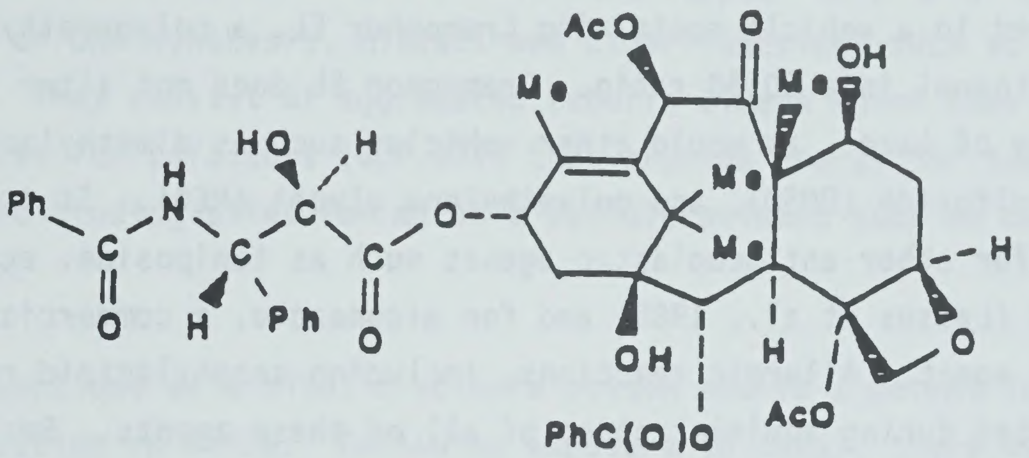
Taxol is a novel diterpene compound extracted from the bark of a western yew, *Taxus brevifolia*. In 1977, taxol was chosen for development as an antineoplastic agent because of its unique mechanism of action and good cytotoxic activity against IP implanted B16 melanoma and the human MX-1 mammary tumor xenograft.

Taxol is believed to function as a mitotic spindle poison and as a potent inhibitor of cell replication *in vitro*. Other mitotic spindle poisons (colchicine and podophyllotoxin) inhibit microtubule assembly. Taxol employs a different mechanism of action in that it appears to shift the equilibrium of polymerization/depolymerization toward polymer assembly and to stabilize microtubules against depolymerization under conditions which would cause rapid disaggregation of microtubules. The interference with the polymerization/depolymerization cycle in cells appears to interfere with both the replication and migration of cells.

Preclinical toxicology studies were performed in CD_2F_1 mice, Sprague-Dawley rats and beagle dogs. In the rodent species, the intraperitoneal route was selected due to dose volume constraints imposed by limited compound solubility and vehicle toxicity. Lethality studies were performed using a X1 and X5 schedule in rats and a X5 schedule in mice. In these intraperitoneal studies, females were slightly less sensitive than males to taxol based upon a comparison of the LD10 and LD50 values. However, the LD90 values were similar for the two sexes in all cases. Using a single schedule, the defined doses in rats for the combined sexes were 137.88, 205.74 and 306.90 mg/m^2 for the LD10, LD50 and LD90, respectively. The LD10, LD50 and LD90 values in the X5 rats (combined sexes) were 35.64, 51.36, and 73.98 mg/m^2/day, whereas corresponding defined doses in the X5 mice (combined sexes) were 69.60, 82.35 and 97.44 mg/m^2/day. Toxicity was evaluated on the defined dose protocol on both X1 and X5 schedules in beagle dogs given taxol by intravenous infusion.

Using these test systems, the main toxic effects of taxol were most evident in the tissues with high cell turnover: hematopoietic, lymphatic,

PHARMACEUTICAL DATA



Chemical Name: β-(Benzoylamino-α-hydroxy-benzenepropanoic acid, 6,12b-bis (acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12, 12a,12b-dodecahydro-4, 11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz [1,2-b]oxet-9-yl ester, [2aR-[2aα,4β,4aβ,6β,9α(αR*,βS*), 11α,12α,12aα,12bα]]-

Molecular Formula: $C_{47}H_{51}NO_{14}$ M.W.: 853.9

Description: Taxol is a poorly soluble plant product isolated from *Taxus brevifolia.*

How Supplied: Injection, 30 mg, ampule/vial: 6 mg/mL, 5 mL, in polyethoxylated castor oil (Cremophor EL®) 50%, and dehydrated alcohol, USP, in 5mL ampules/vials. THIS SOLUTION MUST BE DILUTED BEFORE USE.

Solution Preparation: Taxol concentrations from 0.3 mg/mL to 1.2 mg/mL may be obtained by diluting the solution with proper volumes of either 0.9% Sodium Chloride Injection, USP, or 5% Dextrose Injection, USP.

CAUTION: PVC bags and sets should be avoided due to appreciable leaching of DEHP.

FORMULATION

Taxol, due to its limited solubility in water, is prepared and administered in a vehicle containing Cremophor EL, a polyoxyethylated castor oil, and ethanol in a 50:50 ratio. Cremophor EL does not alter the stability or activity of taxol, as would other vehicles such as dimethylacetamide (DMA), dimethyl sulfoxide (DMSO), and polyethylene glycol (PEG). It is also used as a vehicle for other antineoplastic agents such as teniposide, echinomycin, and didemnin B (Lassus et al., 1985) and for miconazole, a commercially available antifungal agent. Allergic reactions, including anaphylactoid reactions, have been reported during administration of all of these agents. Because of this, taxol is administered by slow IV infusion and patients are pretreated with H_1 and H_2 receptor blockers and diphenhydramine. For other agents listed, the reactions may be alleviated by administration of diphenhydramine following discontinuation of the drug infusion. In some cases, therapy may be allowed to continue following premedication with steroids, diphenhydramine and H_2 antihistamines such as cimetidine and ranitidine. Table 1 (below) lists the concentration of Cremophor EL used in the preparation of various drugs used clinically.

TABLE 1

CREMOPHOR EL CONCENTRATION IN INVESTIGATIONAL DRUGS

Drug	Cremophor EL (ml)/Unit of Drug	Phase II Dose Drug/m^2	Phase II Dose Cremophor EL/m^2
Teniposide	.05/mg	165 mg	8.25 ml
Echinomycin	.00025/µg	2 mg	.5 ml
Taxol	.08/mg	250 mg	20.0 ml
Didemnin B	.03/mg	6.3 mg	0.19 ml
Miconazole	.01/mg	200-1200 mg/infusion (total dose)	2-12 ml/ infusion

Cremophor El has significant inherent toxicity and seems to be much better tolerated when used in a fractionated-dose regimen in dogs. When administered as such, the vehicle had no apparent cumulative toxicity. However, when the

MECHANISM OF ACTION

Microtubules are cellular structures which appear to play a role in initiation of DNA synthesis, mitosis and other functions such as cell migration. They consist of aggregated tubulin dimers which have distinct binding sites for cofactors (GDP,GTP) that provide energy for tubulin assembly and specific binding sites for mitotic spindle poisons such as colchicine and vinblastine.

Taxol functions as a mitotic spindle poison and is a potent inhibitor of cell replication *in vitro*. Following exposure to taxol, there was an increase in the mitotic index of P388 cells (Fuchs and Johnson, 1978) and growth arrest of human HeLa and mouse fibroblast cells in the G_2 and M phases of the cell cycle (Schiff et al., 1979; Schiff and Horwitz, 1980). Although this inhibition is thought to be secondary to a taxol-induced disruption of mitotic spindle function, the drug acts in a manner unique from that of other known mitotic inhibitors. Unlike other plant-derived toxins, such as colchicine and podophyllotoxin, which inhibit microtubule assembly, taxol promoted the assembly of calf-brain microtubules *in vitro* and stabilized these microtubules against depolymerization by either low temperatures or calcium chloride, conditions which normally cause rapid disaggregation of microtubules (Schiff et al., 1978; Schiff et al., 1979). Taxol apparently induces the formation of microtubule polymerization by shifting the tubulin dimer-polymer equilibrium towards polymer assembly and by elimination of the lag period prior to tubulin assembly.

Experiments suggest that taxol has a single, saturable tubulin binding site (Manfredi et al., 1982). Taxol has been shown to inhibit replication of mouse fibroblast cells. Carney et al. (1986) demonstrated that taxol inhibits microtubule depolymerization caused by colchicine, growth factors (epidermal growth factor) and oncogenic DNA viruses (cytomegalovirus, CMV); this inhibition could be overcome by increasing the concentration of colchicine. Ball et al. (1990) recently reported that while human CMV-initiated cell DNA synthesis is blocked by 10-20 μg/ml taxol, CMV-specific early protein synthesis is not affected.

The cell-kill kinetics and cell cycle effects of taxol on human (A2780) and hamster (CHO) ovarian cells were examined by Lopes et al. (1991). CHO cell blocking was dose-dependent and cells were completely blocked in mitosis (M) at 1-1.5 mcg/ml taxol; 1.6 mcg/ml accumulated almost all CHO cells in G_2-M by 12 hr. Cells entered S without cytokinesis to become tetraploid by 24 hr after treatment. A2780 cells were significantly more sensitive to taxol than were CHO cells.

Resistance to taxol may be related to the classical multi-drug resistance phenotype. A taxol resistant cell line has been developed, J7/TAX-50, which is 800-fold resistant to taxol and cross resistant, but to a much lesser degree, to other tubulin binding agents such as colchicine and vinblastine (Horwitz et al., 1986). The induction of resistance in this particular cell line is thought to be due to a particular phosphoglycoprotein (M.W. 135,000 KD) in the cell membrane (Roy and Horwitz, 1985).

ANTITUMOR ACTIVITY

Taxol was selected for clinical development based upon good activity against the intraperitoneally (IP) implanted B16 melanoma (Table 2) and the subrenally implanted human MX-1 mammary tumor xenograft (Table 3). Optimal increased life spans (ILS) of 131% and 141% were obtained following daily IP treatment with 4.44 and 10 mg/kg, respectively, in B16 melanoma. Following subrenal implantation in athymic mice, subcutaneous (SC) administration of taxol (200 mg/kg d1-10) caused MX-1 mammary tumor regression, while 400 mg/kg inhibited tumor growth by 94%. Moderate activity was noted against the IP implanted L1210 and P388 leukemias. Taxol was less effective against the CX-1 colon and the LX-1 lung tumor xenografts. Taxol was not active against the SC implanted murine $CD8F_1$ mammary and colon 38 carcinomas or the intravenously (IV) implanted Lewis lung carcinoma.

When the IP implanted P388 lymphocytic leukemia system was used to examine the effects of schedule and route of administration on the antitumor activity of taxol, doses were restricted to those which were soluble in the ethanol/Cremophor vehicle (Schiff et al., 1979). Because of this, toxic doses were not achieved with all treatment schedules. When administered orally or IV, taxol was inactive and nontoxic in the range of doses and schedules investigated (Table 4). However, when administered IP, the drug was active in five of six schedules evaluated (Table 5). Based on the maximum ILS attained, equivalent activity (44-45%) was observed with single injections of taxol on days 1-5, days 1-9, or days 1, 5, and 9. At the highest doses which were nontoxic to the control animals, however, there was an increase in antitumor activity as the treatment schedule was extended from 5 to 9 days. A single IP administration of the highest dose (9 mg/kg) tested on day 1 only was inactive and nontoxic; however, a fractionated dose of 6 mg/kg given every 3 hours on day 1 (total dose 48 mg/kg) produced an ILS of 78%, the greatest activity observed in this study. Similarly, administration of fractionated doses also produced greater activity on the intermittent treatment schedules. A single dose of 9 mg/kg on days 1, 5, and 9 (total dose, 27 mg/kg) produced an ILS of 44%; administration of 1.7 mg/kg every 3 hours on days 1, 5, and 9 (total

TAXOL, NSC 125973

TABLE 3 ANTITUMOR ACTIVITY OF TAXOL AGAINST THE HUMAN MX-1 MAMMARY TUMOR XENOGRAFT IMPLANTED BENEATH THE RENAL CAPSULE OF ATHYMIC MICE

Expt. No.	Dose (mg/kg/inj.)	Deaths by Day 11/ Total	Body Weight Change (day 11-day 0) (grams)	Average Tumor Weights (mg) Initial	Final	T/C (%)
23-4001	Control	0/6	0.2	0.50	5.67	
	400	2/3	-7.7	0.50		Toxic
	200	1/3	-7.8	0.52	0.17	-67
	100	1/3	-8.5	0.55	0.68	3
	50	0/3	-7.7	0.45	0.82	7
09-900397	Control	0/15	3.0	0.56	14.17	
	400	1/6	-2.7	0.48	1.24	6
	200	0/6	-1.3	0.41	4.04	27
	100	0/6	1.8	0.59	3.43	21
	50	0/6	0.3	0.53	5.10	34

These experiments were performed at Mason Research Institute (Expt. 23-4001), Worcester, MA, and IIT Research Institute (Expt. 09-900397), Chicago, IL, under the direction of Dr. W. Cobb and Mr. A. Shefner, respectively. On day 0, tumor fragments with an average diameter of 9-12 ocular micrometer units (10 OMU = 1 mm; weight of fragment with a length and width of 10 OMU = 0.5 mg) were implanted beneath the renal capsule of NU/NU Swiss (athymic) mice. Taxol as a suspension in Klucel (hydroxypropylcellulose) was administered s.c. on days 1-10 and tumor measurements were taken on day 11. All length by width measurements were converted to weight by the formula: wt. (mg) = (L x W x W)/2 after converting OMU's to mm's. For positive changes in test tumor weights (i.e. mean T.W. on day 11 - mean T.W. on day 0 was positive), T/C values were calculated from the test tumor weight change/control tumor weight change. For negative changes in test tumor weights (tumors regressed), T/C values were calculated from the test tumor weight change/initial test tumor weight.

DEB 11/29/82

TAXOL, NSC 125973

TABLE 5 DOSE RESPONSE EFFECT OF TAXOL AGAINST THE I.P. IMPLANTED P388 LYMPHOCYTIC LEUKEMIA

Route and Schedule of Administration	Dose (mg/kg/inj.)	Deaths by Day 5	Weight diff.[a] (grams)	ILS (%)	Normal S/T
i.p. Q3H, Q1D, Day 1 only	9.0	5/10	-5.5	Toxic	4/8
	6.0	0/10	-5.4	78	7/8
	4.0	0/10	-2.9	56	8/8
	2.6	0/10	-2.2	37	8/8
	1.7	0/10	-1.6	31	8/8
	1.1	0/10	-1.8	26	8/8
	0	0/10	-1.6	11	8/8
i.p. Q3H, Q4D, Days 1,5,9	9.0	5/10	-5.0	Toxic	0/8
	6.0	0/10	-5.2	Toxic	0/8
	4.0	0/10	-4.1	Toxic	7/8
	2.6	0/10	-1.9	53	8/8
	1.7	0/10	-1.6	60	8/8
	1.1	0/10	-1.6	43	8/8
	0	0/10	-1.6	11	8/8

These experiments (P388 expt. 9438, non-tumored animal expt. 1345) were performed at Arthur D. Little, Inc., Cambridge, MA, under the direction of Mr. I. Wodinsky. See the legend under Table 3 for additional details. There were no long-term (30-day) survivors among the treated tumored animals.

a Weight difference = average body weight change (day 5 - day 1) of test group minus that of control animals.

DEB 11/29/82

contrast, microtubule bundling was associated with cytotoxicity and was reversible in the resistant cells, but was irreversible in the sensitive cells. This microtubule bundling persisted even when the sensitive cells were placed in taxol-free media following incubation with taxol. Based on these results, the authors suggested that microtubule effects may be useful in predicting the therapeutic activity of taxol (Rowinsky et al. 1988).

Twelve human cancer cell lines (4 ovarian, 5 endometrial, 1 cervical, 1 breast, and 1 leiomyosarcoma) and 35 fresh tumor specimens from 4 gynecologic sites (ovary, endometrium, cervix and malignant teratoma) were recently employed to examine filtered (0.2 mcm millipore) versus unfiltered taxol cytotoxicity using an ATP chemosensitivity assay (Untch et al., 1991). Only the unfiltered drug showed a dose related cytotoxicity. With filtered drug, there was a 50-100X reduction in cytotoxicity *in vitro* and total inactivation of taxol toxicity in fresh tumor specimens (based on the IC 50 as determined by median effect analysis). These data should be taken into consideration in all taxol experiments and trials.

The following protocol studies were done at Borriston Laboratories, Inc.:

Mouse range-finding (single I.V. dose)*
Mouse range-finding (split level x3 single I.V. dose)*
Mouse range-finding (five daily I.V. doses)*
Mouse range-finding (single I.P. dose)*
Mouse range-finding and lethality (five daily I.P. doses)
Rat range-finding (single I.P. dose)*
Rat range-finding and lethality (single I.P. dose)
Rat range-finding and lethality (five daily I.P. doses)
Vehicle toxicity determination in beagle dogs (I.V.)
Mouse toxicity (five daily I.P. doses)
Rat toxicity (single I.P. doses)
Rat toxicity (five daily I.P. doses)
Dog toxicity (single I.V. dose)
Dog toxicity (five daily I.V. doses)

Pilot studies (*) above are summarized in Table 6. These studies demonstrated that the IV route was not feasible in rodents.

The LD10, LD50 and LD90 from the mouse and rat IP lethality studies are in Tables 7-9. In these intraperitoneal studies females are slightly less sensitive to taxol than males, based upon a comparison of LD50 and LD10 values; however, the LD90 values were similar for the two sexes in all cases. The rat (on a mg/m^2 basis) was more sensitive than the mouse by a factor of approximately 2; however, the difference in the slopes of the dose response curves was sufficient to suggest possible differences in absorption or metabolism.

Because the IP route was used in rodent studies and due to potential difficulties in extrapolating doses for the dog, IV toxicity studies in the dog were done by the defined dose protocol. In these studies the Lethal Dose (LD), Toxic Dose High (TDH), Toxic Dose Low (TDL), and Highest Non-Toxic Dose (HNTD) were established for both x1 and x5 dose schedules. These doses are presented in Table 10.

TABLE 7

DEFINED DOSES FROM THE FIVE CONSECUTIVE DAILY INTRAPERITONEAL DOSE LETHALITY STUDY IN CD2F1 MICE

SEX	DEFINED DOSE	ESTIMATED DOSE mg/kg/day	ESTIMATED DOSE $mg/m^2/day$	95% CONFIDENCE Limits (mg/kg/day)	Slope and Heterogeneity Factors
Male	LD10	21.57	64.71	19.04-23.05	Slope = 17.66
	LD50	25.50	76.50	24.10-26.78	Heterogeneity = 1.00
	LD90	30.13	90.39	28.45-33.36	
Female	LD10	26.09	78.27	23.97-27.36	Slope = 23.88
	LD50	29.52	88.56	28.30-30.87	Heterogeneity = 1.00
	LD90	33.40	100.20	31.76-36.64	
Combined	LD10	23.20	69.60	21.69-24.28	Slope = 17.54
	LD50	27.45	82.35	26.52-28.40	Heterogeneity = 1.00
	LD90	32.48	97.44	31.07-34.67	

TABLE 8

DEFINED DOSES FROM THE SINGLE INTRAPERITONEAL DOSE LETHALITY STUDY IN SPRAGUE-DAWLEY RATS

	DEFINED DOSE	ESTIMATED DOSE mg/kg	ESTIMATED DOSE mg/m^2	95% CONFIDENCE Limits (mg/kg)	Slope and Heterogeneity Factors
Male	LD10	21.55	129.30	15.40-24.87	Slope = 7.17
	LD50	32.53	195.18	29.21-37-45	Heterogeneity = 1.00
	LD90	49.11	294.66	41.27-75.74	
Female	LD10	26.03	156.18	19.12-29.21	Slope - 9.37
	LD50	35.66	213.96	32.84-39.58	Heterogeneity - 1.00
	LD90	48.86	293.16	42.76-70.74	
Combined	LD10	22.98	137.88	18.53-25.70	Slope = 7.38
	LD50	34.29	205.74	31.92-37.33	Heterogeneity = 1.00
	LD90	51.15	306.90	44.80-66.56	

Due to the sensitivity of the dog to the Cremophor component of the vehicle, and the need to use large infusion volumes, pilot studies were done in dogs to determine the maximum non-lethal volume of vehicle. A maximum of 10 ml/kg/day at 2 ml/min was tolerated on a x5 schedule, while 20 ml/kg at 2 ml/min was tolerated on a x1 schedule; 40 ml/kg at 4 ml/min was lethal to 1/2 dogs and 60 ml/kg at 4 ml/min was lethal to the remaining dog. Toxic signs related to either the Cremophor or ethanol components of the vehicle were observed in all toxicity studies. Additional vehicle control groups (30 ml/kg and 22.5 ml/kg) were added to the x1 study and 50% mortality was observed at these dose levels.

Rodent toxicity studies were done to provide assessment of target organ toxicity in a second species. As previously stated, both rat (x1 and x5) and mouse (x5 only) studies were done. The doses used in these studies are listed in Table 11.

Mouse x5 Intraperitoneal Lethality Study

Clinical signs in this study included lethargy and rapid respiration on days of dosing (attributable to vehicle) and dose-related incidences of rough coat, hunched back and thin appearance. Ataxia, squinted eyes and difficult respiration occurred sporadically. Mean body weight losses of 10-19% were noted in all treated groups except VCTL females during the first five days. Recovery of weight loss occurred by day 19.

Rat Intraperitoneal Lethality Studies (x1 and x5)

Clinical signs, attributable to vehicle, included rapid breathing (x1 study only), prostration and lethargy on the day(s) of dosing. Persistent lethargy, rough coat, soft feces and hunched posture were principal taxol-related signs lasting through days 13 (x1) and 21 (x5). Sporadic incidences of chromodacryorrhea, lacrimation, squinted eyes, and difficult breathing were noted in both studies. Additional findings in x1 included tremors and sneezing and in x5 included prostration, bloody nose, swollen jaws and protruding penis.

TABLE 11 (Cont.)

FIVE CONSECUTIVE INTRAPERITONEAL DOSE TOXICITY STUDY IN SPRAGUE-DAWLEY RATS

Group	Number/ Sex	Dose (mg/kg/day)	Dose mg/m²/day	Cumulative Dose mg/m²	Volume Administered (ml/g/day)	Concentration (mg/ml)
LD50	10/M*	7.47	44.82	224.10	0.05	0.1494
LD10	10/M*	5.11	30.66	153.30	0.05	0.1022
1/2LD10	10/M*	2.55	15.30	76.50	0.05	0.0510
VCTL	10/M	0.00	0.00	0.00	0.05	0.0000
NCTL	10/M	—	—	—	—	—
LD50	10/F	9.99	59.94	299.70	0.05	0.1998
LD10	10/F	8.58	51.48	257.40	0.05	0.1716
1/2 LD10	10/F	4.29	25.74	128.70	0.05	0.0858
VCTL	10/F	0.00	0.00	0.00	0.05	0.0000
NCTL	10/F	—	—	—	—	—

*The doses used for the males on the toxicity study are slightly higher than those calculated by probit analyses. As the differences were less than 10%, no adverse effect on interpretation of the study results is anticipated.

In the x5 dogs, severe lymphoid depletion and necrosis of the tonsils were seen in one-short term dog on the LD. Marked tonsilar lymphoid depletion was noted in the long-term TDH dog. The short-term TDH and long-term TDL dogs had severe to marked purulent inflammation of the tonsils. These lesions are all considered secondary to immunosuppression, and were not reversible in the observation period in these studies.

Persistent inflammation of the mandibular lymph nodes was noted in the long-term taxol-treated rats; this was apparently associated with the neck abscesses observed in lethality and toxicity studies.

Hematopoietic System:

Aside from sporadic hemoconcentration possibly related to dehydration and two occurrences of anemia in the x5 LD50 rats, evidence of erythroid toxicity in rodents was limited to reversible, dose-related decreases in circulating reticulocytes in both species.

Dogs were more affected than rodents. Severe hemoconcentration was observed in the SLD x5 dogs, probably due to dehydration. Effects were not observable in the x1 LD due to the acute deaths of the dogs. Marked anemia was observed at the x1 and x5 TDH dose (x1 nadir day 14, x5 nadir day 22), which reversed by day 43 in both dogs. The intermediate level (4.5 mg/kg) x1 dogs had readily reversible anemia, which was accompanied by marked increases in RBC's on day 8. Dogs at the TDL and HNTD levels showed only mild, readily reversible effects on erythropoietic parameters.

Reticulocyte levels were severely depressed in the x1 TDH and intermediate dose level dogs (nadir day 4), and in the LD and TDH dogs on the x5 schedule (nadir days 4-8). Recovery occurred in the TDH dog.

Thrombocytopenia was observed in the TDH dogs of both schedules, the 4.5 mg/kg x1 dog, and in the SLD and LD x5 dogs. The responses in the x5 dogs were of greater severity. Reversible thrombocytopenia was observed in x5 rats of both sexes at the LD50 and in females at the LD10.

dose groups makes assessment of reversibility difficult although only oligospermia was observed in (1/2) long-term LD10 males examined.

Rats in both schedules showed significantly higher than control relative testicular weights at the short-term sacrifice; only x5 rats had histologic confirmation of a toxic effect, with giant cell formation and necrosis occurring in two LD50 rats. Weight differences were reversible and no lesions were observed in long-term rats.

Cardiovascular System:

No histological evidence of cardiac toxicity was found in these studies and no special cardiovascular studies were performed. However, clinical observations suggest a cardiovascular effect probably related to the vehicle. Acute deaths were observed within one half to one hour after dosing in 2/2 dogs receiving the LD x1 at a dose volume of 30 ml/kg, in 1/2 dogs receiving vehicle at 30 ml/kg and in 2/4 dogs at 22.5 ml/kg. Clinical signs including vasodilation, hypothermia, labored/difficult breathing, and lethargy were observed in these dogs prior to death and are compatible with hypotensive shock. Additionally, contraction of the right ventricle and dilation and flabby appearance of the left ventricle was noted in two vehicle dogs during gross examination at necropsy. Dogs have been previously reported to be sensitive to the hypotensive effects of Cremophor, one of the vehicle components in this study, and the effects noted above correlate with this (Lorenz et al. 1977).

Nervous System:

No histological evidence of drug- or vehicle-related toxicity to the central or peripheral nervous system was seen in any species. Clinical signs suggestive of central effects were noted.

On the day(s) of dosing, lethargy and tachypnea were noted in all dosed x5 mice; lethargy and ataxia were present in LD50 and VCTL x1 rats and lethargy and tachypnea were present in x5 treated and VCTL rats. These signs

reversible; reversibility could not be assessed on the x5 schedule due to deaths of the dogs.

<u>Hepatic</u>:

There was no histological evidence of liver toxicity. Variable responses were seen in liver enzymes (alkaline phosphatase, SGOT, SGPT) and lipid parameters, including cholesterol measured in both rats and dogs, and total lipids and triglycerides which were measured in dogs only.

Mice in LD50 and LD10 groups had low relative liver weights on day 8; reversible increases in SGOT and SGPT were present in these groups. Rats on the x5 schedule showed increased relative liver weights (significant in females only) on day 8 only. Reversible increases were noted in SGOT in x1 LD50 and LD10 rats, and in x5 LD50 female rats. Decreased SGOT was present in the x5 LD50 male rats. Reversible decreases in alkaline phosphatase and SGPT occurred in the x1 LD50 and LD10 rats on day 4, and in the x5 LD50 and LD10 rats on day 8. The biological significance of decreased alkaline phosphatase and SGPT is not clear. Reversible increases in cholesterol were noted in x1 LD50 and LD10 rats and in x5 LD50 rats.

Increases in alkaline phosphatase, SGOT and SGPT occurred in x1 TDH and x5 SLD dogs and were reversible in the x1 dogs. Reversible increases in SGOT also occurred in the x1 intermediate dose level dogs. Increased SGOT and SGPT occurred in the x5 LD dogs, and reversible increases in alkaline phosphatase and SGPT occurred in the x5 LD dogs; reversible increases in alkaline phosphatase and SGPT occurred in the x5 TDH dogs. Vehicle dogs showed reversible increases in alkaline phosphatase and SGPT (x1) and SGPT (x5).

Effects on bilirubin were apparent only in the x5 SLD dogs, in which terminal increases in both total and direct bilirubin occurred.

Cholesterol, total lipids and triglycerides were increased in the x5 SLD dogs and x5 TDH dogs. Cholesterol and total lipids were increased in the x5 LD and x1 TDH; total lipids only were increased in the x1 intermediate level,

and HNTD were minimal, with mild emesis occurring at the TDL and diarrhea at the HNTD. Vehicle control dogs (at 5 ml/kg/day) showed mild emesis and mucoid stool while those in the x5 pilot study at 10 ml/kg/day had more severe signs of emesis and bloody diarrhea. The toxicity seen in the x5 SLD-TDH taxol-treated dogs, however, was of much greater severity and duration.

Histopathologic findings in mice included severe to moderate atypical hyperplasia in the crypts of Lieberkuhn and moderate to severe duodenal necrosis and inflammation in LD50 and LD10 mice. These lesions were reversible as evidenced by their absence in surviving LD10 mice. LD50 and LD10 rats on the x1 schedule showed moderate to severe gastritis, and moderate to severe atypical hyperplasia in the crypts of Lieberkuhn in the duodenum or cecum. Diffuse chronic inflammation of the duodenum and mucoid membrane necrosis were also noted.

No histological evidence of gastrointestinal toxicity was seen in x5 rats except chronic and persistent visceral peritonitis seen in several LD50 rats, probably subsequent to the repeated intraperitoneal injections.

Microscopic examination of dogs showed severe drug-related congestion of the ileum, cecum and colon in one x5 LD dog. Chronic inflammation of the duodenum and inflammation and necrosis of the colon were observed in the short-term x5 TDH dog. No other drug-related gastrointestinal lesions were seen in either dog toxicity study.

Conclusion:

Taxol (NSC-125973) at a maximum concentration of 0.6-0.7 mg/ml 5% Cremophor EL®, 5% ethanol, 90% physiologic saline, could not be given to rodents by the IV route due to dose-volume constraints. IP lethality and toxicity studies were done x5 in CD2F1 mice, and x1 and x5 in the Sprague-Dawley rat. Toxicity was evaluated on the defined dose protocol on both x1 and x5 schedules in beagle dogs given taxol by IV infusion.

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ANNUAL REPORT

TO THE

FOOD AND DRUG ADMINISTRATION

TAXOL

IND 22850

NSC 125973

March 1991

Drug Sponsor:

Division of Cancer Treatment
National Cancer Institute
Bethesda, Maryland

This document contains both published and unpublished data describing the results of clinical trials sponsored by the Division of Cancer Treatment, NCI, with this agent. The unpublished data are preliminary and should not be quoted or used for any purpose other than as guidance in developing clinical trials.

TABLE OF CONTENTS

INTRODUCTION

This annual report to the Food and Drug Administration (FDA) provides an update on the status of clinical trials with taxol (IND 22850, NSC 125973), sponsored by the Division of Cancer Treatment (DCT), the National Cancer Institute (NCI).

Taxol is a novel diterpene compound derived from the bark and needles of the western yew, *Taxus brevifolia*. It was originally isolated by Wani et al. in 1971. In 1977 taxol was chosen for development as an antineoplastic agent because of its unique mechanism of action and good cytotoxic activity against the intraperitoneally (IP) implanted B16 melanoma and the human MX-1 mammary tumor xenograft (Taxol Clinical Brochure, 1990). Taxol inhibits normal cellular replication *in vitro* by promoting microtubule assembly and stabilizing tubulin polymers against depolymerization (Schiff et al., 1979; Kumar, 1981; Schiff and Horwitz, 1981). Clinical trials of taxol sponsored by the DCT, NCI, began in 1983. Data supporting the entries in the clinical trials tables are included in Appendix A. A summary of current preclinical data pertaining to taxol is contained in the Clinical Brochure (Appendix B).

CLINICAL PHARMACOLOGY

Preliminary pharmacokinetic data were reported by investigators from Johns Hopkins and the University of Wisconsin. Although use of a tubulin-dependent biochemical assay was attempted initially by these investigators (Hamel et al., 1982), this assay lacked sufficient sensitivity for analysis of human pharmacokinetic data. Subsequently, a high-performance liquid chromatographic (HPLC) assay was developed which was used for pharmacokinetic studies conducted in conjunction with phase I studies of taxol at Albert Einstein, Johns Hopkins, and the University of Wisconsin (Grem et al., 1987; Longnecker et al.,1987; Wiernik et al., 1987a; Wiernik et al., 1987b; Rowinsky et al., 1989). The dose of taxol administered in these studies ranged from 15-390 mg/m^2, and the infusion and administration schedules ranged from 1 to 24 hours and single dose to daily x 5. Peak plasma levels were variable, ranging between 0.06 and 10 μmol depending on the dose and schedule of administration. Using the dose and schedule selected for phase II trials, peak plasma levels were 0.88 μmol on one

study (Wiernik et al., 1987a) and 1.57 on the second (Rowinsky et al., 1989). Levels were found to vary among patients receiving the same dose. However, the plasma levels do appear to be dose-related. The achievable plasma concentrations in most studies are comparable to the levels required for anti-proliferative effects *in vitro*. Overall, the disappearance of taxol from the plasma appears to be biexponential, with mean terminal half-lives ($t\ 1/2\beta$) ranging from 1.5-8.4 hours, depending on the dose and schedule investigated. Urinary excretion (2.1-6.6%) over 24-48 hours was not substantial, suggesting that other routes of elimination such as biliary may account for systemic clearance of taxol. No metabolites of taxol were found in any of the studies. A detailed description of the pharmacokinetic behavior of intravenous taxol as observed in these studies is presented in Table 1. Pharmacokinetic studies by Markman et al. (1991) of taxol delivered by the intraperitoneal (IP) route showed that the ratio of peak cavity/plasma levels ranges from >150-800 fold; the AUC advantage for IP administration was even larger. Even when taxol was given systemically, cavity levels were much higher than plasma levels.

CLINICAL TRIALS

Phase I

Fourteen DCT, NCI-sponsored phase I trials are being or have been conducted with taxol. No single-agent phase I trials are currently accruing patients; however, two combination trials are open to patient accrual. A phase I trial (T90-0106) in patients with refractory or recurrent ovarian cancer was recently completed; it established 300 mg/m^2 as the MTD of taxol when given with G-CSF (DLT = peripheral neuropathy) and had a 31% response rate (4/13). The MTD of IP taxol (200 mg/m^2) was recently established with refractory ovarian cancer patients (GOG-8808); abdominal pain was the DLT and all other toxicities were described as mild to moderate. Response rate will be available following final evaluation.

One phase I trial (T90-0095) which continues to accrue patients is a follow-up to T88-0166; the new study uses a combination of taxol, cisplatin (CDDP) and G-CSF in solid tumor patients. Investigators are reporting significant amelioration of the severe neutropenia that was associated with the

taxol/CDDP combination encountered in T88-0166. They also report that 2/4 evaluable patients on the new combination have partial responses (PR); both responders are non-small cell lung cancer patients. A phase I trial opened in March 1991 (T90-0232) combines taxol, adriamycin and G-CSF; investigators are seeking the MTD of this combination in previously untreated breast cancer patients.

Taxol has been evaluated on three schedules (Legha et al., 1986; Kris et al., 1986; Donehower et al., 1987). The dx1 bolus schedule was not taken into phase II trials because of the high incidence of hypersensitivity reactions. The incidence of these was reduced by lengthening the infusion time. In T87-0053, 31 patients received taxol over 6 hours without premedication. Only one hypersensitivity reaction was reported. This is a much lower incidence than reported for the trials using a shorter infusion period (Table 5). Two trials using the dx5 bolus and one using the 5 day continuous infusion schedule every three or four weeks were performed. No responses were observed on any of these trials. Three single agent trials were done using a 24 hour continuous schedule every 3 weeks. Because of the responses seen and the low incidence of hypersensitivity reactions, this schedule was selected to be taken into phase II trials.

Myelosuppression, primarily leukopenia, was the dose-limiting toxicity on most early trials. Hypersensitivity was treatment-limiting on one of the single bolus trials, and a combination of neurotoxicity and myleosuppression was limiting on another (Lipton et al., 1989). One of the 24 hour infusion trials reported neurotoxicity as dose-limiting, and the phase I trial in leukemia patients reported mucositis as the dose-limiting toxicity. Details of the phase I trials can be found in Table 2.

Responses were observed on two schedules in the phase I trials. Partial responses were seen in lung, ovary and an adenocarcinoma of unknown origin on the single bolus schedule. On the 24 hour infusion schedule, responses were reported in several sites: melanoma, AML, head and neck, colon, ovary, lung (in combination with CDDP) and in adenocarcinomas of unknown primaries.

Phase II

There are six phase II trials of taxol currently accruing patients (Table 3). These are trials in cancer of the upper GI tract (T86-0164), lung (small cell, EST-1590; non-small cell lung, EST-1589 and T87-0006), ovary (T90-0219) and prostate (EST-1890). T90-0219 is an extention of studies begun in T90-0106; investigators are seeking to determine if response rates in ovarian cancer are higher at 250 mg/m^2 than those reported for 135-175 mg/m^2. In addition, there are two trials which have closed accrual, but have patients continuing to receive taxol. These are in metastatic breast cancer (T86-0270) and colon cancer (EST-P-A286). In the active phase II trials taxol is being administered at a dose of 135-250 mg/m^2 as a 24-hour CIV infusion every 3 weeks; patients are premedicated with diphenhydramine, dexamethasone, and a histamine H_2 receptor blocker (either cimetidine or ranitidine). Recently a phase II trial in metastatic breast cancer has been approved; it seeks confirmation of encouraging results seen in T86-0270.

Previously, responses have been reported in untreated melanoma (12%) (Legha et al., 1990), and in heavily pretreated ovarian (30%) cancer patients (McGuire et al, 1989). In a study (GOG-26FF) which closed in 1989 final analysis of data showed that 36% of 42 patients with advanced or recurrent ovarian carcinoma responded. Duration of response ranged from 6-25 months, averages were 8 months (8 PR) and 9 months (7 CR); 21 patients had stable disease for 3-11 months. No responses were reported in previously untreated renal carcinoma (Einzig et al., 1988); mean survival time for these patients was 7 months (Walpole et al., 1991). Response rates in recently closed and ongoing phase II trials are 56% (14/25) for patients with previously treated metastatic breast cancer (T86-0270) and 13% (2/15) for non-small cell lung cancer (T87-0006). Eight of the 14 responding patients on T86-0270 have shown no evidence of relapse or recurrence more than one year after their initial response.

Phase III

Because of the high response rate obtained in previously treated ovarian cancer patients, a phase III study (GOG-111) of Cytoxan/CDDP versus taxol/CDDP is ongoing (Table 4). Untreated ovarian cancer patients are randomized to receive either 750 mg/m^2 Cytoxan and 75 mg/m^2 CDDP or 135 mg/m^2 of taxol and 75

mg/m^2 CDDP every 3 weeks. The doses of taxol and CDDP in combination were developed in a pilot trial at Johns Hopkins (T88-0166).

TOXICITY

Acute Allergic Reactions

Acute allergic reactions, characterized by anaphylactoid or urticarial reactions, have occurred in several patients treated with taxol in phase I and phase II trials (see Tables 2 and 3).

In an effort to minimize episodes of allergic reactions, a letter was sent in January 1985, to all phase I investigators using taxol with the following recommendations: 1) all patients should be pretreated with both steroids and antihistamines; 2) the minimum duration of infusion should be 6 hours; 3) during the first 30 minutes of the 6-hour infusion, drug should be delivered at a 24-hour CIV rate; and, 4) if no reaction occurs during the first 30 minutes, the rate of infusion should be changed so that the remainder of drug is delivered in 5.5 hours. Additional warning letters were sent to investigators in May and June 1985 reiterating these recommendations.

All phase II trials of taxol utilize a 24-hour CIV schedule of administration in conjunction with premedication. The premedication regimen currently recommended for all patients who receive taxol includes dexamethasone 20 mg orally (PO) 14 hours and 7 hours prior to taxol, cimetidine 300 mg IV and diphenhydramine 50 mg IV 30 minutes prior to therapy.

The incidence of severe allergic reactions has been reduced in the later trials which employed both a longer duration of infusion and premedication. On one phase I trial (T87-0053), taxol was administered IV over 6 hours without premedication. Only one hypersensitivity reaction was reported in 31 patients, suggesting that an infusion of this length is tolerable without premedication.

Other Toxicities

The dose-limiting toxicity on most trials, regardless of schedule, has been myelosuppression (primarily leukopenia). Peripheral neuropathy has been reported to be dose-limiting on two solid tumor trials (T84-0195 and T87-0053). When a sural nerve biopsy was taken from a patient who had been receiving taxol for 12 months (cumulative dose = 6603 mg), severe nerve fiber loss, axonal atrophy and secondary demyelination, possibly indicative of a cell body disease, were observed (New et al., 1991). Mucositis was dose-limiting on the leukemia trial (T85-0240). Other toxicities include alopecia, nausea and vomiting, fatigue, local venous reactions, myalgia, ahd arthralgia. Allergic reactions including flushing, skin rash, and/or pruritus have also been observed.

In November 1987, a warning letter was sent to all investigators using taxol concerning cardiac arrhythmia in a 60-year-old patient with metastatic ovarian carcinoma (no known history of organic heart disease). Because of the possibility of anaphylactoid reactions, all patients in this study (T85-0277) underwent cardiac monitoring during drug administration. Although this patient showed no abnormalities prior to the start of her second cycle (135 mg/m^2, 24 hr CIV), within 8 hours she was noted to have Mobitz type I and II arrhythmias. Approximately 15 hours into the infusion, the patient remained asymptomatic, but was in complete A-V block, with asystole lasting 7.5 seconds. Taxol was discontinued, and a temporary transvenous pacemaker was inserted. She had persistent episodes of complete A-V block during the next 48 hours, and underwent placement of a permanent pacemaker. The mean terminal half-life of taxol on the 24 hour CIV schedule is reported to be 3.3 hours (Table 1). Because the A-V conduction abnormalities in this patient continued so long after the termination of the taxol infusion, it is unlikely that this arrythmia was related to the administration of taxol. A second patient experienced trigeminy approximately 1 hour after the initiation of a 24 hour infusion of taxol; however, this quickly resolved and the patient tolerated the remainder of the infusion without any additional arrhythmias. In four phase I and II studies at Johns Hopkins Oncology Center between 1983 and 1990, 5% (7/140) of patients on taxol experienced cardiac disturbances; these included brady- and tachyarrhythmias, atrioventricular and bundle branch blocks, and cardiac ishemia (Rowinsky et al., 1991).

In September, 1990, another warning letter was sent to taxol investigators concerning several episodes of ventricular tachycardia (VT) during or following taxol in combination with cisplatin. Four chemotherapy naive patients experienced brief periods of asymptomatic VT in the absence of electrolyte disturbances. None had a history of cardiac disease, and the episodes were not associated with a specific dose, duration of infusion, or number of courses. Electrolyte and cardiac monitoring are now recommended for all patients participating in combination taxol/cisplatin trials.

ADVERSE DRUG REACTIONS +

ADR No./		Assessment			
(Protocol No.)	Reaction	IND Drug	Non-IND Drug	Disease	Other
90-07-108 (T88-0166)	Cardiac dysrhythmia	Probable	Unlikely		
90-07-109 (T88-0166)	Cardiac dysrhythmia	Probable	Unlikely		
90-07-110 (T88-0166)	Cardiac dysrhythmia	Probable	Unlikely		
90-07-111 (T88-0166)	Cardiac dysrhythmia	Probable	Unlikely		
90-08-123 (T90-0106)	Heart block	Possible	Unlikely	Unlikely	
90-09-145 (T88-0166)	Nausea/vomiting, hypotension	Possible	Probable	Possible	Probable
90-09-146 (T88-0166)	Nausea/vomiting, hypotension	Unlikely	Probable	Unlikely	Probable
91-01-05 (EST-1589)	Cardiac, edema, orthapnea	Possible		Possible	
91-02-23 (EST-1589)	Pulmonary edema, lung infiltrates	Possible	Unlikely		
91-03-78 (T90-0106)	Submental pain, parasthesias	Unrelated			
91-03-83 (EST-1489)	Anxiety, depression, taste perversion	Possible		Possible	Probable

ADVERSE DRUG REACTIONS +

ADR No./ (Protocol No.)	Reaction	Assessment IND Drug	Non-IND Drug	Disease	Other
90-12-H30* (GOG-111)	Infection, atrial fibrillation	Possible	Unlikely		Possible
90-12-H68* (EST-1589)	Chest pain	Unlikely			Definite
91-01-H73* (GOG-111)	Hypomagnesia, hypocalcemia	Unrelated	Definite		
91-01-H74* (EST-1589)	Cardiac ischemia, myocard. infarct.	Unrelated			
91-02-H22* (EST-1589)	Death	Unrelated		Probable	
91-02-H35* (EST-P-A286)	Anaphylaxis	Definitely		Unlikely	
91-02-H78A* (EST-1589)	Diarrhea	Probable			
91-02-H78B* (EST-1589)	Death	Unlikely		Probable	
91-03-H13* (T90-0095)	Cardiac dysrythymia	Probable	Possible		
91-03-H18* (EST-P-A286)	Hepatic - bilirubin	Unrelated		Definite	
91-03-H19* (EST-1589)	Death	Unrelated		Definite	
91-03-H58* (EST-1589)	Polyarthralgia, pancytopenia	Probable			
91-03-H83* (GOG-111)	Hematologic	Definite	Possible		

+ Reported since submission of the preceding Annual Report to the FDA in March 1990.
* Not previously reported to the FDA.

SUMMARY AND PLANS

The phase I trials with taxol on the d x 1 and d x 5 schedules are closed. Several phase I 24 hour CIV trials remain open. An unacceptably high incidence (11%, 13/117) of acute allergic reactions occurred when taxol was given as a short ($\leq$ 6 hours) IV infusion during the initial phase I studies. Consequently, all phase II trials of taxol with the current formulation have been undertaken with the 24-hour CIV schedule together with premedication, typically diphenhydramine, cimetidine, and dexamethasone. This schedule was chosen because of both its low incidence (2.9%, 3/105) of acute allergic reactions in phase I and preclinical data which showed maximal activity when taxol was administered IP every 3 hours on day 1 to mice with SC implanted P388 leukemia.

A limited number of pilot trials of taxol in combination with one other active agent will be sought late in 1991 to determine the MTD of these combinations and the recommended phase II dose of active doublets. These trials will be performed with patients who have platinum-refractory ovarian cancer.

Taxol is derived from a lengthy extraction of bark obtained from the western yew, *Taxus brevifolia*. This process requires about two years and a large volume of the raw material to produce relatively small amounts of drug. The possibility of preparing a synthetic version of taxol has been studied without success thus far. The limited drug supply has proven to be a major obstacle in the development of this compound. Additional drug has become available recently, enabling the activation of limited trials. Phase II trials in a number of sites will be activated as drug supply permits. Pediatric phase I trials in both leukemia and solid tumors have been initiated. Further IP phase I work will continue in order to optimize a schedule for early-stage ovarian disease patients.

Major efforts by the NCI and pharmaceutical industry are ongoing in an effort to develop a reliable source of this compound for future clinical use. The DCT, NCI, plans to keep the IND for taxol open to support a broad clinical evaluation.

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TABLE 1

TAXOL PHARMACOKINETICS[1]

Protocol #/ Institution	Dose mg/m^2	Schedule	# Pts.	C_{max}	AUC	t 1/2 α	t 1/2 β	CL_{TB}	V_d	CL_R	MRT	24h Urinary Excretion % dose	Reference
T83-1052 Johns Hopkins	15-265	1h IV d x 1 6h IV d x 1	19	2.2-13.0 μM	47-5833 μM min	16.2 ± 9.4 min	6.4 ± 3.9 h	253 ± 274 $ml/min/m^2$	67.1 ± 54.7 L/m^2	29.3 ± 39.7 $ml/min/m^2$	5.6 h (335 ± 218 min)	5.9 ± 8.8[2]	Am J Path 112:207, 1983
T84-0195 Albert Einstein	175-275	6h IV d x 1	12	5.17 μM	29.9 h mg/L	21.6 min (0.36 h)	8.3 h	135 $ml/min/m^2$	59.2 L/m^2	7.0 $ml/min/m^2$	7.7 h	5.1	Cancer Res 45:3856, 1985
	200-275	24h CIV	9	0.79 μM	11.6 h mg/L	20.4 min (0.34 h)	3.3 h	359 $ml/min/m^2$	119 L/m^2	--	17.4 h	2.1	The Prostate 11:95, 1987
T83-0995 U. Wisc	15-40	1h IV d x 5 6h IV d x 5	8	225 ng/ml	38.6 min mg/L	--	1.4 h (86 ± 44 min)	53 ± 28 $L/h/m^2$	81 ± 32 L/m^2	--	--	6.6	An NY Acad Sci 466:733, 1986
T87-0053 San Antonio	175-275	6h IV d x 1	8	1.41-4.10 μg/ml	8.06-27.97 μg h/ml	0.51 ± 0.3 h	3.8 ± 2.0 h	13.9 ± 4.7 $L/h/m^2$	42.91 ± 8.74 L/m^2		2.92 ± 1.4 h		Contract Rep. 11/89
T85-0240 Johns Hopkins (Leukemia)	250 315 390	24 hr CIV		1.57±0.29 2.93±0.42 3.50±1.43 μg/ml	--	--	--	--	--	--	--	--	Proc AACR CR 28:423, 1987

[1]Not all parameters were measured in every patient; see references for details. Data represent mean values.
[2]Over 48 hours
C_{max}: Peak plasma concentration
AUC: Area under concentration-time curve
t 1/2: Plasma half-life
CL_{TB}: Total body clearance
V_d: Volume of distribution
CL_R: Renal clearance
MRT: Mean residence time

TABLE 2

TAXOL PHASE I TRIALS

Protocol No. Inst./PI	Schedule	Dose mg/m^2 Lowest	Dose mg/m^2 Highest	Dose mg/m^2 MTD	Dose mg/m^2 Recommended Phase II Dose	# Pts. Ent.	Toxicity	Reference/Status
T83-1051 MDA Legha	1 h IV d x 5 q 3 wk	5	40	30	30	20	DLT: leukopenia Other: mild N&V, stomatitis, alopecia, diarrhea, weakness, fatigue, local rash	Schedule not to be taken into Phase II J Clin Oncol 4:762, 1986 Completed 3/85
T83-0995 Univ. of Wisconsin Trump	1 h or 6 h IV d x 5 q 4 wk	5	40	40	30	16	DLT: leukopenia Gr 3: fatigue Other: N&V, alopecia, elev. BUN, plt, anaphylactoid reactions, sore throat, pruritic rash, elev. liver enzymes, infection, ulcer, oral mucosa	No anaphylactoid reactions observed in the premedicated pts. who received the 6h IV. Schedule not to be taken into Phase II Cancer Treat Rep 71:1179, 1987 Completed
T84-0194 DFCC Spriggs	24 h CIV d x 5 q 3-4 wk	5	36	36	30	20	DLT: myelosuppression, leukopenia-(Grade 4-25% at highest doses), N&V Other: N&V, diarrhea, mucositis, infection	Schedule not to be taken into Phase II Pers. Comm. 4/87 Completed

%: Percent of courses
CIV: Continuous Intravenous Infusion

TABLE 2 (continued)

TAXOL PHASE I TRIALS

Protocol No. Inst./PI	Schedule	Dose mg/m² Lowest	Highest	MTD	Recommended Phase II Dose	# Pts. Ent.	Toxicity	Reference/Status
T83-0991 MSKCC Kris	3 h IV d x 1 q 3 wk	15	230	--	--	17	Treatment-limiting: Hypersensitivity-3/5 pts. at ≥ 190 mg/m² (Grade 5-1 pt., incl.) Other: N&V, stomatitis, rash, malaise, diarrhea, alopecia, elev. serum triglycerides	Schedule will not be taked into Phase II because of the 18% incidence of hypersensitivity reactions. Cancer Treat Rep 70:605, 1986 Completed
T83-1052 Johns Hopkins Ettinger	1 h or 6 h IV d x 1 q 3 wk	15	265	265	Minimal prior therapy: 212 Extensive prior therapy: 170	30	DLT: Leukopenia Gr 3-4: WBC, plt, mucositis Other: peri. neuro., N&V, hypersensitivity, alopecia, double vision, local venous, myalgia/ arthralgia	Schedule will not be taken into Phase II 2 PR: NSCL, ovarian. Cancer Treat Rep 71:53, 1987 (pharmacokinetics) Cancer Treat Rep 71:1171, 1987 Completed

TABLE 2 (continued)

TAXOL PHASE I TRIALS

Protocol No. Inst./PI	Schedule	Dose mg/m^2 Lowest	Highest	MTD	Recommended Phase II Dose	# Pts. Ent.	Toxicity	Reference/Status
T84-0195 Albert Einstein Einzig	1-6 h IV d x 1 q 3 wk 24 h CIV d x 1 q 3 wk	15 150	275 275	275 275	250 250	34 26	dx1 bolus DLT: neurotoxicity and leukopenia Gr 3-4: hematologic, neurologic, alopecia, Other: allergic, N&V, stomatitis, dyspnea, rash 24h CIV DLT: peri. neuro. Gr 3-4: WBC, peri. neuro. Other: hypersensitivity, rash/pruritis/flushing	d x 1 bolus schedule not to be taken into Phase II Cancer Res 47:2486, 1987 J. Clin Oncol 5:1232, 1987 d x 1 bolus 1 PR: unknown adenocarcinoma 24h CIV 4 PR/12: melanoma Completed
T83-1197 Mt. Sinai Ohnuma	24 h CIV q 3 wk	15	300	–	–	42	Leukopenia, anaphylaxis, alopecia, N&V, stomatitis, diarrhea, transient hepatic, transient azotemia, malaise, pruritis,	Schedule taken into Phase II AACR 26:167, 1985 CTMS Rep. 4/87 Pers. Comm. 2/86 Completed

TABLE 2 (Continued)

TAXOL PHASE I TRIALS

Protocol No. Inst./PI	Schedule	Dose mg/m² Lowest	Highest	MTD	Recommended Phase II Dose	# Pts. Ent.	Toxicity	Reference/Status
T85-0240 Johns Hopkins Donehower (Leukemia)	24 h CIV q 3 wk	200	400	390	315	17	DLT: mucositis Gr 3-4: fever, GI tract, Hgb, WBC, plt, mucositis, weight loss, hepatic, bleed, musculoskeletal, peri. neuro., pulmonary, renal, weight gain Other: alopecia, cutaneous, cardiac, diarrhea, N&V, neuro, weakness	Contr. Rep. 12/88 CTMS Rep. 1/89 1 PR: ALL Cancer Res 49:4640-4647, 1989 Closed 7/88
T87-0053 San Antonio Brown	6h IV q 3 wk	175	275	275	Untreated pts: 250 Previously treated pts.: 200	31	DLT: myelosuppression and peri. neuro. Gr 3-4: cardiac, GI tract, WBC, seizure, weight loss, hepatic, plt, mucositis, musculoskeletal, PS Other: allergic, alopecia taste, anorexia, cutaneous, ↑ BP-1, fatigue, fever, diarrhea, N&V, GU, headache, Hgb, metab., neuro., peri. neuro., renal, temp. change	Patients on this trial were not premedicated. Contr. Rep. 12/89 3 PR: 1 NSCL (3 months), 2 unknown primary (2,3+ months) Completed 2/89
T88-0166 Johns Hopkins Rowinsky	q 3 wks Taxol 24h CIV	110	200	200	High Risk 135 Low Risk 170	44	DLT: neutropenia Other: alopecia, fever, N&V, diarrhea, thrombocytopenia, myalgias, arthralgias, hypersensitivity, hearing loss, neuro., bradycardia, ventricular tachycardia	Open 1989. Order of admin. of taxol or CDDP was alternated. Taxol should precede CDDP 2 CR, 8 PR. Phase I Mtg. Min. 3/91. Closed 12/90.
	CDDP 1 mg/min IV	50	75	75	75			
GOG-8808 GOG Hoskins (Ovarian)	50 mg/m² IP q 3 wks	25	200	200	–	25	DLT: abdominal pain Other: myelosuppression, allergic reactions	ASCO 10:185, 1991 GOG Report 2/91. Personal Comm 3/91. Closed 3/91.

TABLE 2 (continued)

TAXOL PHASE I TRIALS

Protocol No. Inst./PI	Schedule	Dose mg/m² Lowest	Dose mg/m² Highest	Dose mg/m² MTD	Dose mg/m² Recommended Phase II Dose	# Pts. Ent.	Toxicity	Reference/Status
T90-0095 Johns Hopkins Rowinsky	q 3 wks Taxol 24 hr CIV	135	170	–		5	Neutropenia, thrombocytopenia, ventricular ectopy, N&V, alopecia, fever	Open 10/90. Phase I Mtg Minutes 3/91. 2 PR: NSCLC
	CDDP 1 mg/min IV	75	75			–		
	G-CSF 5 μg/kg/d SC							
T90-0106 NCIMB Reed (Ovarian)	q 3 wks Taxol 24 hr CIV	200	300	300	250	13	Granulocytopenia, thrombocytopenia, peri. neuro., alopecia, myalgia, asymp. bradycardia	Open 9/90. Phase I Mtg. Minutes 3/91. 1 CR, 3 PR, 5 SD.
	G-CSF 10 μg/kg/d SC 24 hrs post Taxol							
T90-0232 NCI MB O'Shaughnessy (Breast)	q 3 wks Taxol 72 hr CIV	160						Open 3/91.
	Adriamycin 72 hr CIV	45						
	G-CSF 10 μg/kg/d SC 24 hrs post CIV (d5)							

TA 3
TAXOL PHASE II TRIALS

Disease	Protocol/ Institution	Dose & Schedule	# Pts. Eval. [Ent.]	Response CR	PR	%	Toxicity	Status/Source
Breast (metastatic)	T86-0270 MDA Holmes	250 mg/m^2 24 h CIV q 3 wks	25 [25]	3	11	56	Gr 3-4: Granulocytopenia, fatigue, myalgia, peri. neuro, infection. Other: Diarrhea, alopecia, stomatitis, N&V, arthralgia, anorexia, dysgeusia, constipation, motor, cheilitis, skin, mood, dysuria	Proc ASCO 10:60, 1991 Study Summary Report 2/91 Pers. Comm 3/91 Closed 9/90
Cervical	GOG-76S GOG McGuire	170 mg/m^2 24 hr CIV q 3 wk	29 [32]	0	4	14	Gr 3-4: leukopenia, neutropenia, Hgb, alopecia, pulmonary, infection Other: thrombocytopenia, GI tract, renal, hepatic, fever, neuro., cutaneous	GOG Report 2/91 NPCT Closed 5/90
Colon	EST-P-A286 ECOG Einzig	250 mg/m^2 24 hr CIV q 3 wk	[20]		N.B		N.B.	Open 11/89 NPCT Personal Comm 3/91 Temp Closed 2/91
GI (upper GI tract)	T86-0164 Einstein Wiernik	250 mg/m^2 24 hr CIV q 3 wk	5 [5]	0	0		Gr 5: pulmonary-1 Gr 3-4: WBC, Hgb, granulocytopenia, neutropenia, infection, bilirubin neuro-sensory Other: plt, transaminase, alopecia	Open 1/90 $\leq$ 1 PCT Study Summary Report 2/91 Will become EST 8290
Bronchogenic (NSC)	EST-1589 ECOG Chang	250 mg/m^2 24 hr CIV q 3 wk	[25]	-	N.B.	-	Gr 3-4: leukopenia, diarrhea, cardiac, allergic, neuro.	Open 2/90 NPCT ECOG Min. 6/91 Personal Comm. 3/91
(SCLC)	EST 1590 ECOG Ettinger	250 mg/m^2 24 hr CIV q 3 wk	[9]		N.B.	--	N.B.	Open 8/90 Personal Comm. 3/91 ECOG Min. 6/91
NSCLC	T87-0006 MDA Dhingra	250 mg/m^2 24 hr CIV q 3 wks	15 [16]	0	2	13	Gr 3-5: Granulocytopenia, leukopenia, alopecia, plt Other: edema, dyspnea, N&V, stomatitis, headache, bone pain, Hgb, infection, diarrhea, fatigue, sensory, fever, BP	Open 12/89 Study Summary Report 2/91
Melanoma	EST-P-A686 ECOG Einzig	250 mg/m^2 24 h CIV q 3 wk	28 [34]	2	2	14	Gr 3-4: WBC, infection, anaphylactoid neuropathy, infection Other: diarrhea, alopecia, stomatitis/ mucositis, phlebitis	NPCT ASCO 7:249, 1988 ECOG Min. 6/87 Pers. Comm. 2/89 Closed 2/87
	T86-0262 MDA Legha	250 mg/m^2 24h CIV q 3 wk	25 [25]	0	3	12	Gr 3-4: gran, infection, alopecia, pain, arthralgia, fever, diarrhea Other: WBC, N&V, malaise, dygeusia, stomatitis, paresthesia, skin rash, pruritus, myalgia	NPCT No prior IL-2 LAK Final Study Summary 6/89 Investigators recommend 200 mg/m^2 due to myelosuppression PR duration 8 17 months DLT-neutropenia Completed 4/89

N.B. = Data are preliminary and have not been reviewed by ECOG.

TABLE 3 (continued)

TAXOL PHASE II TRIALS

Disease	Protocol/ Institution	Dose & Schedule	# Pts. Eval. [Ent.]	Response CR	PR	%	Toxicity	Status/Source
Melanoma	T86-0259 UMCC Van Echo	250 mg/m^2 24h CIV q 3 wk	4 [4]	0	0	0	Gr 3-4: WBC, pulmonary, allergy hepatic Other: Hgb, infection, nausea, stomatitis, alopecia, cardiac, fever	NPCT No prior high-dose IL-2 Final Study Summary 2/88 Completed 10/88
Ovarian	T85-0277 Hopkins McGuire	Good risk: 170 mg/m^2 24 h CIV Poor risk: 135 mg/m^2 24 h CIV	40 [47]	1	11	30	Gr 3-4: WBC, gran, stomatitis, creat., cardiac, CNS, Mg^{++}, plt, Hgb, gran, hemorrhage, infect., hepatic, skin, allergy, arthralgia/myalgia Other: N&V, GI, alopecia, pulmonary, skin, fever, peri. neuro. malaise, restless	All pts. refractory to CDDP. Study Summary 1/89 AACR 28:423, 1987 (cell kinetics) ASCO 7:136, 1988 Closed 7/88
	T86-0233 Einstein Einzig	250 mg/m^2 24h CIV q 3 wk	30 [34]	2	4	20	Gr 3-4: WBC, plt, gran, lymph., infection, Hgb, neuro. Other: N&V, diarrhea, stomatitis, alopecia, fever, local	$\leq$ 1 PCT No prior IL-2 LAK Final Study Summary 2/91 Closed 1/90
	GOG-26FF Thigpen	Good risk: 170 mg/m^2 24 h CIV q 3 wk Poor risk: 135 mg/m^2 24 h CIV q 3 wk	42 [49]	7	8	36	Gr 3-4: WBC, plt, neutropenia, pulmonary, Hgb, alopecia, Other: GI, renal, SGOT, alk phos, infection, GU, cardiac, fever, neurotox	$\leq$ 1 PCT GOG Stat Report 2/91 Closed 7/89
	T90-0219 NCI-MB Reed	250 mg/m^2 24 hr CIV q 3 wk	–	–			–	Open 3/91
Prostate	EST-1890 ECOG Roth	Taxol 135-170 mg/m^2 24 hr CIV q 3 wk G-CSF 5 µg/kg/d SC	[9]		N.B.	–	N.B.	Open 6/90 Personal Comm. 3/91 ECOG Min 6/91
Renal	T86-0163 Einstein Wiernik	250 mg/m^2 24 h CIV q 3 wk	18 [18]	0	0	0	Gr 3-4: WBC, peripheral neuropathy Other: fever, alopecia-18	NPCT AACR 29:222, 1988 Cancer Cen. Rep. 3/88, 8/88 Pers. Comm. 3/88 Closed 7/87

TA[illegible]

TAXOL PHASE III TRIALS+

Disease	Protocol/ Institution	Dose & Schedule	# Pts. Eval. [Ent.]	Response CR	PR	%	Toxicity	Status/Source
Ovarian (Stage III and IV)	GOG-111	Regimen I CDDP 75 mg/m^2 IV d1 q 21 d CTX 750 mg/m^2 IV d1 q 21 d vs Regimen II Taxol 135 mg/m^2 24 hr CIV d1 q 21 d CDDP 75 mg/m^2 24 hr CIV d2 q 21 d	[80]	Too early		–	Too early	Open 4/90 Both measure and non measurable disease. All pts NPCT, NPXRT GOG Report 2/91 Personal Comm. 3/91.

TABLE

INCIDENCE OF ALLERGIC REACTIONS IN TAXOL SINGLE AGENT PHASE I TRIALS

Institution/ Protocol #	Schedule	# Pts. Ent./ [# Pts. Premedicated]	# Pts. with Reactions (# Pts. with Acute Reactions*)			
			Unknown	1st Exposure	2nd Exposure	Total
MSKCC T83-0991	IV d 1 (3 h)	17 [0]	2 (0)	2 (2)	1[a] (1)	5 (3)
Albert Einstein T84-0195	IV d 1	Total: 60 [54]				
	(<6 h)	6 [0]	0	0	3[b] (3)	3 (3)
	(6 h)	28 [28]	0	2 (0)	1 (0)	3 (0)
	(24 h)	26 [26]	7 (0)	0	1 (1)	8 (1)
Johns Hopkins T83-1052	IV d 1	Total: 30 [14]				
	(1 h)	16 [0]	0	2 (1)	3 (3)	5 (4)
	(6 h)	14 [14]	0	0	3 (1)	3 (1)
MDA T83-1051	IV d x 5 (1 h)	20 [0]	2 (0)	0	0	2 (0)
U. Wisc. T83-0995	IV d x 5	Total: 16 [7]				
	(1 h)	9 [0]	0	1 (1)	1 (1)	2 (2)
	(6 h)	7 [7]	0	0	1 (0)	1 (0)
Mt. Sinai T83-1197	24 h (CIV)	42 [0]	0	1 (1)	0	1 (1)
DFCC T84-0194	d x 5 (CIV)	20 [**]	0	0	0	0
John Hopkins T85-0240	24 h (CIV)	17 [17]	0	1 (1)	0	1 (1)
San Antonio T87-0053	IV d1 (6h)	31 [0]	0	0 (0)	1 (1)	1 (1)
Total		253 [92]	11 (0)	9 (6)	15 (11)	35 (17)

*Includes anaphylactoid reactions (shortness of breath, hypotension, and skin rash) which occurred at the onset of infusion.
**This protocol was later amended to include premedication. Although the majority of patients were most likely not premedicated, the number who received premedication is unknown.
[a]Irreversible cardiopulmonary arrest in one patient
[b]Allergic reaction occurred twice in one patient, although this patient was premedicated before being rechallenged.

3/13/92

TAXOL PHASE I TRIALS

NCI PROTOCOL		PATIENTS ACCRUED		
T83-1051		20		
T83-0995		16		
T84-0194		20		
T83-0991		17		
T83-1052		30		
T84-0195		60		
T83-1197		42		
T87-0053		31		
POG-9171		14	(ped. solid tumors)	
T91-0099		4	(solid tumors)	
				254
T85-0240		17	(leukemia)	
CCG-0903		8	(ped. leukemia)	
				25
GOG-8808		25	(IP ovarian)	
GOG-9101		10	(IP ovarian)	
T90-0106	(+G-CSF)	15	(ovarian)	
				50
T88-0166	(+CDDP)	44		
T90-0095	(+CDDP,G-CSF)	32		
T90-0232	(+adria,G-CSF)	25	(ovarian)	
T91-0074	(+adria)	12	(breast)	
				113
		442		

TAXOL PHASE II TRIALS 3/13/92

	NCI PROTOCOL	PATIENTS	RESPONSE DATA
BREAST	T86-0270	25	56% response, JNCI 83:1797, 1991
	T91-0009	26	62% response, ASCO, 1992
CERVICAL	GOG-76S	29	14% response
COLON	EST-P-A286	19	No response
GI, UPPER	EST-8290	18	Too early
HEAD/NECK	EST-P-A390	17	Too early
LUNG	T87-0006 (NSCLC)	25	24% response, ASCO, 1992
	EST-1589 (NSCLC)	24	21% response, ASCO, 1992
	EST-1590 (SCLC)	18	
MELANOMA	EST-P-A686	28	14% response, ASCO 7:249, 1988
	T86-0259	4	
	T86-0262	25	12% response, Cancer 65:2478, 1990
OVARIAN	GOG-26FF	41	36% response, ASCO 9:604, 1990
	T85-0277	40	30% response, ASCO 7:136, 1988
	T86-0233	29	21% response, AACR 31:1114, 1990
	T90-0219	55	Response data under review
PROSTATE	EST-1890	23	4% response, ASCO, 1992
RENAL	T86-0163	18	No responses, AACR 29:222, 1988
		464	

TREATMENT REFERREL CENTER PROTOCOL

OVARIAN	TRC-9103	957	21% response, Emmes Report (preliminary, based upon first 90 patients evaluable for response)

TAXOL PHASE III TRIALS

OVARIAN	GOG-111	196	Too early for response data

3/13/92

THE FOLLOWING TAXOL STUDIES HAVE BEEN APPROVED

	LOI/PROTOCOL	APPROX. ACCRUAL GOAL
Phase I		
	L91-0544	30 (pharmacokinetics in patients with abnormal liver function)
	T92-0017	30 (4 d CIV and drug resistance mechs. in patients with breast cancer or lymphoma)
BREAST	T92-0059	30 (+RT followed by standard chemotherapy)
	L91-0496	30 (+CTX, pharmacologic)
OVARIAN	L91-0335	30 (+CDDP)
	L91-0393	30 (+CBDCA)
	L91-0395	30 (+Ifosfamide)
	L91-0396	30 (+VP-16)
	L91-0397	30 (+Topotecan)
	L91-0408	30 (+CDDP/CBDCA/G-CSF)
	T91-0168	30 (+CDDP/CTX/G-CSF)
	T92-0014	30 (+HMM)
Phase II		
BLADDER	EST-8-04	30
BREAST	T92-0061	30 (heavily pretreated)
CNS	T91-0265	30
ENDOMETRIAL	L91-0504	40
ESOPHAGEAL	L91-0461, L91-0471	30 (will be conducted as one trial)
HEAD/NECK	L92-0009	30
LIVER	L92-0030	30
LUNG (SCLC)	L91-0510	30
	L91-0536	30
LYMPHOMA	L91-0085	30 (+chemosensitizer)
	L92-0033	30
MESOTHELIOMA	L91-0497	30
MYELOMA	L91-0327	30
NEUROENDOCRINE	L91-0545	30
PANCREATIC	SWOG-9135	30
SARCOMA	SWOG-9134	30
TESTICULAR	L89-0166	30
	L91-0415	30
Phase III		
BREAST	CR 91-032	300 (taxol vs adria vs taxol+adria)
OVARIAN	GOG-132	400 (taxol vs CDDP vs taxol+CDDP)
	T91-0117	60 (taxol vs hydroxyurea [IND pending])
		1670

Planned Studies (to be activated during 1992)

BREAST	000-0000	140 (taxol vs vinblastine)
	000-0000	600 (24 hr vs 3 hr taxol infusion)
OVARIAN	L92-0000	660 (randomized, 3 taxol dose levels)
		1400

NUMBER OF 30 MG VIALS OF TAXOL DISTRIBUTED/YEAR
FROM CTEP DRUG MANAGEMENT AND AUTHORIZATION SECTION

1984	1,890
1985	2,350
1986	3,477
1987	4,587
1988	5,636
1989	4,726
1990	12,564
1991	32,412
1992 (1/1-2/10)	12,041
Total	79,683

TAXOL PHASE I TRIALS

Protocol No. Inst./PI	Schedule	Dose mg/m² Lowest	Highest	MTD	Recommended Phase II Dose	# Pts. Ent.	Toxicity	Reference/Status
T83-1051 MDA Legha	1 h IV d x 5 q 3 wk	5	40	30	30	20	DLT: leukopenia Other: mild N&V, stomatitis, alopecia, diarrhea, weakness, fatigue, local rash	Schedule not to be taken into Phase II J Clln Oncol 4:762, 1986 Completed 3/85
T83-0995 Univ. of Wisconsin Trump	1 h or 6 h IV d x 5 q 4 wk	5	40	40	30	16	DLT: leukopenia Gr 3: fatigue Other: N&V, alopecia, elev. BUN, plt, anaphylactoid reactions, sore throat, pruritic rash, elev. liver enzymes, infection, ulcer, oral mucosa	No anaphylactoid reactions observed in the premedicated pts. who received the 6h IV. Schedule not to be taken into Phase II Cancer Treat Rep 71:1179, 1987 Completed
T84-0194 DFCC Spriggs	24 h CIV d x 5 q 3-4 wk	5	36	36	30	20	DLT: myelosuppression, leukopenia-(Grade 4-25% at highest doses), N&V Other: N&V, diarrhea, mucositis, infection	Schedule not to be taken into Phase II Pers. Comm. 4/87 Completed
T83-0991 MSKCC Kris	3 h IV d x 1 q 3 wk	15	230	--	--	17	Treatment-limiting: Hypersensitivity-3/5 pts. at $\geq$ 190 mg/m^2 (Grade 5-1 pt., Incl.) Other: N&V, stomatitis, rash, malaise, diarrhea, alopecia, elev. serum triglycerides	Schedule will not be taked into Phase II because of the 18% incidence ofhypersensitivity reactions. Cancer Treat Rep 70:605, 1986 Completed
T83-1052 Johns Hopkins Ettinger	1 h or 6 h IV d x 1 q 3 wk	15	265	265	Minimal prior therapy: 212 Extensive prior therapy: 170	30	DLT: Leukopenla Gr 3-4: WBC, plt, mucositis Other: peri. neuro., N&V, hypersensitivity, alopecla, double vision, local venous, myalgla/ arthralgia	Schedule will not be taken into Phase II 2 PR: NSCL, ovarian. Cancer Treat Rep 71:53, 1987 (pharmacokinetics) Cancer Treat Rep 71:1171, 1987 Completed

%: Percent of courses
CIV: Continuous intravenous infusion

TAXOL PHASE I TRIALS (continued)

Protocol No. Inst./PI	Schedule	Dose mg/m^2 Lowest	Highest	MTD	Recommended Phase II Dose	# Pts. Ent.	Toxicity	Reference/Status
T84-0195 Albert Einstein Einzig	1-6 h IV d x 1 q 3 wk 24 h CIV d x 1 q 3 wk	15 150	275 275	275 275	250 250	34 26	dx1 bolus DLT: neurotoxicity and leukopenia Gr 3-4: hematologic, neurologic, alopecia Other: allergic, N&V, stomatitis, dyspnea, rash 24h CIV DLT: peri. neuro. Gr 3-4: WBC, peri. neuro. Other: hypersensitivity, rash/pruritis/flushing	d x 1 bolus schedule not to be taken into Phase II Cancer Res 47:2486, 1987 J. Clin Oncol 5:1232, 1987 d x 1 bolus 1 PR: unknown adenocarcinoma 24h CIV 4 PR/12: melanoma Completed
T83-1197 Mt. Sinai Ohnuma	24 h CIV q 3 wk	15	300	--	--	42	Leukopenia, anaphylaxis, alopecia, N&V, stomatitis, diarrhea, transient hepatic, transient azotemia, malaise, pruritis	Schedule taken into Phase II AACR 26:167, 1985 CTMS Rep. 4/87 Pers. Comm. 2/86 Completed
T85-0240 Johns Hopkins Donehower (Leukemia)	24 h CIV q 3 wk	200	400	390	315	17	DLT: mucositis Gr 3-4: fever, GI tract, Hgb, WBC, plt, mucositis, weight loss, hepatic, bleed, musculoskeletal, peri. neuro., pulmonary, renal, weight gain Other: alopecia, cutaneous, cardiac, diarrhea, N&V, neuro, weakness	Contr. Rep. 12/88 CTMS Rep. 1/89 1 PR: ALL Cancer Res 49:4640-4647, 1989 Closed 7/88
T87-0053 San Antonio Brown	6h IV q 3 wk	175	275	275	Untreated pts: 250 Previously treated pts.: 200	31	DLT: myelosuppression and peri. neuro. Gr 3-4: cardiac, GI tract, WBC, seizure, weight loss, hepatic, plt, mucositis, musculoskeletal, PS Other: allergic, alopecia taste, anorexia, cutaneous, ↑ BP-1, fatigue, fever, diarrhea, N&V, GU, headache, Hgb, metab., neuro., peri. neuro., renal, temp. change	Patients on this trial were not premedicated. Contr. Rep. 12/89 3 PR: 1 NSCL (3 months), 2 unknown primary (2,3+ months) Completed 2/89
T88-0166 Johns Hopkins Rowinsky	q 3 wks Taxol 24h CIV CDDP 1 mg/min IV	110 50	200 75	200 75	High Risk 135 Low Risk 170 75	44	DLT: neutropenia Other: alopecia, fever, N&V, diarrhea, thrombocytopenia, myalgias, arthralgias, hypersensitivity, hearing loss, neuro., bradycardia, ventricular tachycardia	Open 1989. Order of admin. of taxol or CDDP was alternated. Taxol should precede CDDP 2 CR, 8 PR. Phase I Mtg. Min. 3/91. Closed 12/90.
GOG-8808 GOG Hoskins (Ovarian)	50 mg/m^2 IP q 3 wks	25	200	200		25	DLT: abdominal pain Other: myelosuppression, allergic reactions	ASCO 10:185, 1991 GOG Report 2/91. Personal Comm 3/91. Closed 3/91.

TAXOL PHASE I TRIALS (continued)

Protocol No. Inst./PI	Schedule	Dose mg/m^2 Lowest	Highest	MTD	Recommended Phase II Dose	# Pts. Ent.	Toxicity	Reference/Status
T90-0095 Johns Hopkins Rowinsky	q 3 wks Taxol 24 hr CIV	135	170	--		32	Neutropenia, thrombocytopenia, ventricular ectopy, N&V, alopecia, fever	Open 10/90. Phase I Mtg Minutes 3/91.
	CDDP 1 mg/min IV	75	75					
	G-CSF 5 μg/kg/d SC							
T90-0106 NCIMB Reed (Ovarian)	q 3 wks Taxol 24 hr CIV	200	300	300	250	15	Granulocytopenia, thrombocytopenia, peri. neuro., alopecia, myalgia, asymp. bradycardia	Open 9/90. Phase I Mtg. Minutes 3/91.
	G-CSF 10 μg/kg/d SC 24 hrs post Taxol							
T90-0232 NCIMB O'Shaughnessy (Breast)	q 3 wks Taxol 72 hr CIV	160				25		Open 3/91.
	Adriamycin 72 hr CIV	45						
	G-CSF 10 μg/kg/d SC 24 hrs post CIV (d5)							
CCG-0903 CCSG Seibel (Ped. leukemia)	24 h CIV, q 3 wk					8	Too early	Open 8/91
GOG-9101 GOG Markman (Ovarian)	IP. q 3 wk					10	Too early	Open 10/91
POG-9171 POG Hurwitz (Ped solid tumors)	24 h CIV, q 3 wk					14	Too early	Open 6/91
T91-0074 MDA Holmes (Breast)	24 hr CIV, q 3 wk + Adria + G-CSF					12	Too early	Open 8/91
T91-0099 Einstein Einzig (solid tumors)	24 hr CIV, q 3 wk + G-CSF					4	Too early	Open 1/92

TAXOL PHASE II TRIALS

Disease	Protocol	Dose & Schedule	# Pts. Ev. [Ent]	Response CR	PR	Rate	Toxicity	Status/Source
Breast (metastatic)	T86-0270 MDA Holmes	250 mg/m^2 h CIV q 3 wks	25 [25]	3	11	56	Gr 3-4: Granulocytopenia, fatigue, myalgia, peri. neuro, infection Other: Diarrhea, alopecia, stomatitis, N&V, arthralgia, anorexia, dysguesia, constipation, motor, chelitis, skin, mood, dysuria	Proc ASCO 10:60, 1991 Study Summary Report 2/91 Pers. Comm 3/91 JNCI 83:1797, 1991 Closed 9/90
	T91-0009 MSK Reichman	250 mg/m^2 24 hr CIV q 3 wk + G-CSF	26 [28]	1	15	62	Too early	Open 4/91 ASCO, 1992
Cervical	GOG-76S GOG McGuire	170 mg/m^2 24 hr CIV q 3 wk	29 [32]	0	4	14	Gr 3-4: leukopenia, neutropenia, Hgb, alopecia, pulmonary, infection Other: thrombocytopenia, GI tract, renal, hepatic, fever, neuro., cutaneous	GOG Report 2/91 NPCT Closed 5/90
Colon	EST-P-A286 ECOG Einzig	250 mg/m^2 24 hr CIV q 3 wk	19 [20]	0	0		N.B.	NPCT Personal Comm 3/91 Closed 2/91
GI (upper GI tract)	EST-8290 ECOG Wiernik	250 mg/m^2 24 hr CIV q 3 wk	18 [18]	N.B.			Gr 5: pulmonary-1 Gr 3-4: WBC, Hgb, granulocytopenia, neutropenia, infection, bilirubin, neuro-sensory Other: plt, transaminase, alopecia	Open 1/90 ≤ 1 PCT Study Summary Report 2/91
Head and Neck	EST-P-A390 ECOG Forastiere	250 mg/m^2 24 hr CIV q 3 wk + G-CSF	14 [17]				Too early	Open 3/91
Lung (NSC)	EST-1589 ECOG Chang	250 mg/m^2 24 hr CIV q 3 wk	24 [25]	--	5	21	Gr 3-4: leukopenia, diarrhea, cardiac, allergic, neuro	NPCT ECOG Min. 6/91 ASCO, 1992 Closed 8/91
(SCLC)	EST 1590 ECOG Ettinger	250 mg/m^2 24 hr CIV q 3 wk	18 [36]	N.B.		--	N.B.	Personal Comm. 3/91 ECOG Min 6/91 Closed 10/91
(NSC)	T87-0006 MDA Dhingra	250 mg/m^2 24 hr CIV q 3 wks	25 [27]	1	5	24	Gr 3-5: Granulocytopenia, leukopenia, alopecia, plt Other: edema, dyspnea, N&V, stomatitis, headache, bone pain, Hgb, infection, diarrhea, fatigue, sensory, fever, BP	ASCO, 1992 Closed 9/91

NB - Data are preliminary and have not been reviewed by ECOG

TAXOL PHASE II TRIALS (continued)

Disease	Protocol	Dose & Schedule	# Pts. Ev. [Ent]	Response CR	Response PR	Response Rate	Toxicity	Status/Source
Melanoma	EST-P-A686 ECOG Einzig	250 mg/m^2 24 h CIV q 3 wk	28 [34]	2	2	24	Gr 3-4: WBC, Infection, anaphylactoid, neuropathy, Infection Other: diarrhea, alopecla, stomatitis/mucositls, phlebitls	NPCT ASCO 7:249, 1988 ECOG Min. 6/87 Pers. Comm. 2/89 Closed 2/87
	T86-0262 MDA Legha	250 mg/m^2 24 h CIV q 3 wk	25 [25]	0	3	12	Gr 3-4: gran, Infection, alopecia, pain, arthraliga, fever, diarrhea Other: WBC, N&V, malaise, dysgeusia, stomatitis, paresthesia, skin rash, pruritus, myalgia	NPCT No prior IL-2 LAK Final Study Summary 6/89 Investigators recommend 200 mg/m^2 due to myelosuppression PR duration 8-17 months DLT neutropenia Completed 4/89 Cancer 65:2478, 1990
	T86-0259 UMCC Van Echo	250 mg/m^2 24 h CIV q 3 wk	4 [4]	0	0	0	Gr 3-4: WBC, pulmonary, allergy, hepatic Other: Hgb, infection, nausea, stomatitis, alopecia, cardiac, fever	NPCT No prior high-dose IL-2 Final Study Summary 2/88 Completed 10/88
Ovarian	T85-0277 Hopkins McGuire	Good risk: 170 mg/m^2 24 h CIV Poor risk: 135 mg/m^2 24 h CIV	40 [47]	1	11	30	Gr 3-4: WBC, gran, stomatitis, creat., cardiac, CNS, Mg^{++}, plt, Hgb, gran, hemorrhage, infect., hepatic, skin, allergy, arthralgla/myalgia Other: N&V, GI, alopecia, pulmonary, skin, fever, peri. neuro. malalse, restless	All pts. refractory to CDDP Study Summary 1/89 AACR 28:423, 1987 (cell kinetics) ASCO 7:136, 1988 Closed 7/88
	T86-0233 Einstein Einzig	250 mg/m^2 24 h CIV q 3 wk	29 [34]	2	4	21	Gr 3-4: WBC, plt, gran, lymph., infection, Hgb, neuro Other: N&V, diarrhea, stomatltls, alopecla, fever, local	$\leq$ 1 PCT No prior IL-2 LAK AACR 31: 1114, 1990 Closed 1/90
	GOG-26FF Thigpen	Good risk 170 mg/m^2 24 h CIV q 3 wk Poor risk: 135 mg/m^2 24 h CIV q 3 wk	42 [49]	7	8	36	Gr 3-4: WBC, plt, neutropenia, pulmonary, Hgb, alopecla Other: GI, renal, SGOT, alk phos, infection, GU, cardlac, fever, neurotox	$\leq$ 1 PCT GOG Stat Report 2/91 ASCO 9:604, 1990 Closed 7/89
	T90-0219 NCI-MB Reed	250 mg/m^2 24 hr CIV q 3 wk + G-CSF	14 [55]				--	Open 3/91
	TRC 9103 NCI-CTEP Arbuck	135 mg/m^2 24 hr CIV q 3 wk	90 [957]	3	16	21	Gr 4: WBC-58, plts-8, N&V-6, infect.-10, cardiac-2, allergic-1, other-8 Gr 3: WBC-68, plts-11, N&V-9, stomatitis-1, infect.-14, neuro-sens.-5, other-11	Open 8/91 Treatment-related deaths - 3

TAXOL PHASE II TRIALS (continued)

Disease	Protocol	Dose & Schedule	# Pts. Ev. [Ent]	Response CR	PR	Rate	Toxicity	Status/Source
Prostate	EST-1890 ECOG Roth	Taxol 135-170 mg/m ^{2} 24 hr CIV q 3 wk G-CSF 5 μg/kg/d SC	23 [23]	1	--	4	N.B.	Personal Comm. 3/91 ECOG Min 6/91 ASCO, 1992 Closed 5/91
Renal	T86-0163 Einstein Wiernik	250 mg/m ^{2} 24 h CIV q 3 wk	18 [18]	0	0	0	Gr 3-4: WBC, peripheral neuropathy Other: fever, alopecia-18	NPCT AACR 29:222, 1988 Cancer Cen. Rep 3/88, 8/88 Pers. Comm. 3/88 Closed 7/87

TAXOL PHASE III TRIALS[+]

Disease	Protocol/ Institution	Dose & Schedule	# Pts. Ev. [Ent]	Response CR	Response PR	Response %	Toxicity	Status/Source
Ovarian (Stage III and IV)	GOG-111	Regimen I CDDP 75 mg/m^2 IV d1 q 21 d CTX 750 mg/m^2 IV d1 q 21 d vs Regimen II Taxol 135 mg/m^2 24 hr CIV d1 q 21 d CDDP 75 mg/m^2 24 hr CIV d2 q 21 d	[196]	Too early			Too early	Open 4/90 Both measure and non measurable disease. All pts NPCT, NPXRT GOG Report 2/91 Personal Comm. 3/92 Accrual closed

List of Funded Taxol Grants for FY 1992

:rant Number	P.I., Institution and Title	Total Costs	% Taxol	Taxol Costs
1 CA 12115-22*	Leo A. Paquette The Ohio State University "Cytotoxic, Carcinogenic, and Antileukemic Agents"	$ 207,341	20	$ 41,468
1 CA 16318-18*	Robert Schimke Stanford University "Molecular Mechanism in Resistance to Folate Analogues"	$ 250,176	5	$ 12,509
7 CA 22215-15	Yoshito Kishi Harvard University "Synthesis of Antitumor Natural Products"	$ 298,819	20	$ 59,764
1 CA 26376-13	Richard F. Luduena University of Texas "Mechanism of Action of Antitumor Drugs"	$ 174,644	10	$ 17,464
1 CA 31845-12	Paul A. Wender Stanford University "Synthetic Studies Related to Cancer Research/Treatment"	$ 549,279	60	$ 329,567
5 CA 39821-08*	Susan Horwitz Yeshiva University "Antitumor Drugs--Mechanisms of Action and Resistance"	$ 874,063	15	$ 131,109
1 CA 41349-07*	Charles Swindell Bryn Mawr College "Synthesis of Taxinine and Taxol"	$ 177,834	100	$ 177,834
1 CA 42031-08*	Robert Holton Florida State University "Total Synthesis of Antitumor Taxanes"	$ 276,798	100	$ 276,798

rant Number	P.I., Institution and Title	Total Costs	% Taxol	Taxol Costs
1 CA 48974-03*	David Kingston Virginia Polytechnic Institute and State University "Photoaffinity Labeling of Tubulin by Taxol"	$ 97,987	100	$ 97,897
1 CA 52790-03*	Gunda Georg University of Kansas "Semisynthetic Taxol Derivatives"	$ 103,189	100	$ 103,189
1 CA 52962-11*	Fernando Cabral University of Texas, Houston "Genetic Approach to Microtubule Function in CHO Cells"	$ 231,232	20	$ 46,246
4 CA 53060-03*	Paul Grothaus Hawaii Biotechnology Group, Inc. "Immunoassays for Taxol"	$ 104,958	100	$ 104,958
1 CA 55102-02*	John Aynsley Escagenetics Corporation "Production of Taxol by Plant Tissue Culture"	$ 296,208	100	$ 296,208
5 CA 55111-01**	Timothy L. Macdonald University of Virginia "Taxol Interactions with Microtubules and Tubulin"	$ 0		$ 0
1 CA 55106-02*	David D. Ellis University of Wisconsin "Taxol Production Utilizing a Nodule Culture System"	$ 148,645	100	$ 148,645
1 CA 55118-02*	Ching-jer Chang Purdue University "Taxol and Taxanes from Plant Tissue Culture"	$ 252,345	100	$ 252,345
1 CA 55127-02*	James D. McChesney University of Mississippi "Development of Reliable and Economic Sources of Taxol"	$ 143,895	100	$ 143,895

rant Number	P.I., Institution and Title	Total Costs	% Taxol	Taxol Costs
1 CA 55131-02*	David G. Kingston Virginia Polytechnic Institute and State University "Enhancement of Taxol's Anticancer Activity and Supply"	$ 218,132	100	$ 218,132
1 CA 55133-02*	Eric K. Rowinsky The Johns Hopkins Oncology Center "Human Metabolism of Taxol"	$ 313,218	100	$ 313,218
1 CA 55138-02*	Michael L. Shuler Cornell University "Manipulation of T. brevifolia"	$ 354,564	100	$ 354,564
1 CA 55139-02*	Charles S. Swindell Bryn Mawr College "Chemical Studies of Taxol and Microtubules"	$ 156,589	100	$ 156,589
1 CA 55148-02*	Yoshito Kishi Harvard University "Synthetic Studies Towards Taxol and Related Compounds"	$ 81,176	100	$ 81,176
1 CA 55150-02*	Nicholas C. Wheeler Weyerhaeuser Company "Genetic Improvement and Cultivation of Yew for Taxol"	$ 116,959	100	$ 116,959
1 CA 55151-02*	Rick G. Kelsey USDA "Culture, Physiology, Genetics, Influencing Taxane Yields"	$ 50,000	100	$ 50,000
5 CA 55159-01**	Bernard Erlanger Columbia University "Immunologic Approaches to Studies of Taxol"	$ 0		$ 0
1 CA 55251-02*	Robert M. Straubinger State University of New York/Buffalo "Pharmacology and Efficacy of Novel Taxol Formulations"	$ 175,192	100	$ 175,192

:rant Number	P.I., Institution and Title	Total Costs	% Taxol	Taxol Costs
)1 CA 55254-02*	Rodney B. Croteau Washington State University "Biosynthesis of Taxol"	$ 145,719	100	$ 145,719
15 CA 56933-01	Paul Sampson Kent State University "Taxol Analogue Synthesis: A Transannular Approach"	$ 96,076	100	$ 96,076
13 CA 57087-01	Paul G. Grothaus Hawaii Biotechnology Group, Inc. "Taxol Purification by Monoclonal Antibody Immunoadsorbents"	$ 50,000	100	$ 50,000
13 CA 57099-01	David C. Muchmore Bend Research Inc. "Novel Enzymatic Approach to Semi-Synthesis of Taxol"	$ 49,700	100	$ 49,700
55 CA 57139-01**	John R. Peterson Panlabs, Inc. "Taxol Molecular Mimics and Photoreactive Analogs"	$ 0		$ 0
JBTOTAL				$4,097,221

:stimates Based on Projected Direct Costs from Current Notice of Grant Award.
*James A. Shannon Director's Award (2 Year Awards, FY 1991 Funds)

July 27, 1990

REQUEST FOR APPLICATIONS for Research Project (R01) Grants

90-CA-16

BIOLOGICAL AND CHEMICAL STUDIES OF TAXOL

NATIONAL CANCER INSTITUTE

APPLICATION RECEIPT DATE: October 24, 1990

LETTER OF INTENT RECEIPT DATE: September 17, 1990

A. INTRODUCTION

The Division of Cancer Treatment (DCT) of the National Cancer Institute (NCI) invites grant applications from interested investigators for chemical and/or biological studies on taxol ultimately leading either to ways to increase production of this drug or to define further its biological properties for use in improved drug design or in enhanced clinical utility.

Grants are awarded to non-profit and for-profit organizations and institutions, governments and their agencies, and occasionally to individuals. The Request for Application's (RFA) is the type of grant solicitation used when it is desired to encourage investigator-initiated research projects in areas of special importance to the National Cancer Program. Applicants funded under the RFA are supported through the customary National Institutes of Health (NIH) grant-in-aid, in accordance with Public Health Service (PHS) policies applicable to research project grants. However, the RFA solicitation represents a single solicitation, with specific deadlines for receipt of applications. All applications received in response to the RFA will be reviewed by the same NCI initial review group.

The present RFA announcement is for a solicitation in FY 1990 with a specified deadline (October 24, 1990) for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements described in the following sections:

*This program is described in the Catalog of Federal Domestic Assistance number 13.395. Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Sections 301, Public Law 78-410, as amended, 42 U.S.C. 241, as amended by Public Law 99-158, 42 U.S.C. and 285(a). This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

B. BACKGROUND INFORMATION

Taxol is an antitumor drug isolated from the Western Yew, Taxus brevifolia, and other Taxus species which has shown excellent confirmed activity against refractory human ovarian cancer and preliminary activity at other sites; it is one of the most promising new drugs in many years. It has a wholly novel mechanism of action, binding to microtubules and stabilizing them against depolymerization. Investigations of the chemistry, biology, biochemistry, and pharmacology of taxol have been limited and many aspects of drug action and of drug production in the source plants, Taxus species, are not well understood.

C. RESEARCH GOALS AND SCOPE

The intention of this RFA is to encourage investigators to propose ideas which will increase our knowledge of the drug's properties and which are likely in the long term to contribute to large scale drug supply and to maximally effective usage of taxol in the clinical setting. The following are undeveloped or underdeveloped areas of interest which merit particular attention: (1) biosynthesis and its regulation in Taxus sp.; (2) plant tissue culture to produce taxol and related compounds; (3) agronomics and plant genetics of taxol to enhance production; (4) evaluation of genetic engineering methods to transfer genes involved in taxol biosythesis to fast growing plants; (5) identification of the specific taxol binding site on microtubules and of the amino acid sequences involved, leading to high resolution definition of the binding site and eventually to molecular mimics with simpler structures; (6) frequency, mechanisms, and circumvention of resistance; (7) studies of in vitro combinations of taxol with other cytotoxic agents; (8) metabolism of taxol in human tissue; (9) measurements and consequences of tissue distribution of taxol; and (10) in vivo evaluation of combination therapy using taxol in preclinical models. These areas are not meant to be restrictive and investigator initiated proposals in all areas of taxol research relevant to the goals of this RFA such as total chemical synthesis are encouraged. Either single or multidisciplinary approaches may be proposed as appropriate to the topic area (see also Section I, INQUIRIES).

The NCI is able to supply limited amounts of taxol for these investigations (up to 100mg. per award). Investigators needing substantial amounts of taxol for proposed studies should contact the Program Director before preparing an application (see Section I, INQUIRIES).

Studies which use taxol as a reagent to isolate microtubules or to study microtubule or cycloskeletal function without therapeutic intent will not be considered responsive to this RFA.

D. MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) grant-in-aid. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Except as otherwise stated in this RFA, awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement, DHHS Publication No. (OASH) 82-50,000, revised January 1, 1987.

This RFA is a one-time solicitation. Generally, future unsolicited competing renewal applications will compete with all investigator initiated applications and be reviewed by the Division of Research Grants (DRG). However, should the NCI determine that there is a sufficient continuing program need, NCI may announce a request for renewal applications. Only recipients of awards under this RFA will be eligible to apply.

Approximately $1,000,000 in total costs per year for five years will be committed to fund applications which are submitted specifically in response to this RFA. It is anticipated that five to eight awards will be made. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Program balance among various areas of taxol/Taxus research will be an important funding consideration.The total project period for applications submitted in response to the present RFA should not exceed five years. Foreign grants are limited to a three year project period. The earliest feasible start date for the initial awards will be July 1, 1991. Although this program is provided for in the financial plans of the National Cancer Institute (NCI), the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

E. ELIGIBILITY REQUIREMENTS

Domestic and foreign non-profit and for-profit institutions are eligible to apply. Governments and their agencies are also eligible.

F. REVIEW PROCEDURES AND CRITERIA

REVIEW PROCEDURE

Upon receipt, applications will be reviewed intially by the Division of Research Grants (DRG) for completeness. Incomplete applications will be returned to the applicant without further consideration. Evaluation for responsiveness to the RFA is an NCI program staff function. Applications will be judged to determine how well they meet the goals and objectives of the program as described in the RFA. Applications judged non-responsive will be returned by the NCI, but may be submitted as investigator-initiated research grants at the next receipt date. Questions concerning the relevance of proposed research to the RFA should be directed to program staff as described in the INQUIRIES section.

In cases where the number of applications is large compared to the number of awards to be made, the NCI may conduct a preliminary scientific peer review to eliminate those applications which are clearly not competitive. The NCI will remove from competition those applications judged to be noncompetitive for award and notify the applicant and institutional business official.

Those applications judged to be both competitive and responsive will be further evaluated according to the review criteria stated below for scientific and technical merit by an appropriate peer review group convened by the Division of Extramural Activities, NCI. The second level of review by the National Cancer Advisory Board considers the special needs of the Institute and the priorities of the National Cancer Plan.

REVIEW CRITERIA

The factors considered in evaluating the scientific merit of each response to this RFA will be:

1. The degree of importance of the research to one of the following:

   a. understanding and/or enhancement of taxol production;

b. mechanism of activity of taxol as an antitumor agent; and

c. potential enhancement of clinical utility of taxol.

2. The originality of the research plan from a scientific and technical viewpoint.

3. Adequacy, thoroughness, and completeness of the scientific plan.

4. Experience, training and time commitment of the Principal Investigator and staff.

5. Adequacy and availability of laboratory space and equipment required.

6. Clearly demonstrated access to all materials (i.e., chemicals, reagents, biological samples, human tissues, etc.) as are needed for the research.

The review group will critically examine the submitted budget and will recommend an appropriate budget and period of support for each approved application.

G. METHOD OF APPLYING

The most recent revision of the regular research grant application form PHS 398, (Revised 10/88) must be used in applying for these grants. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, Maryland 20892; or from the NCI Program Director named below.

The RFA label available in the October 1988 revision of Application Form PHS 398 must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of your application such that it may not reach the review committee in time for review. In addition, the RFA number and title should be typed on line 2 of the face page of the application form.

Submit a signed, typewritten original of the application, including the Checklist, and four (4) signed, exact photocopies, in one package to the address below. The photocopies must be clear and single sided.

DIVISION OF RESEARCH GRANTS
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, Maryland 20892

At time of submission, send two (2) additional copies of the application to:

REFERRAL OFFICER
Division of Extramural Activities
National Cancer Institute
Room 838, Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20892

Applications must be received by October 24, 1990. If an application is received after that date, it will be returned. If the application submitted in response to this RFA is substantially similar to a research grant application already submitted to the NIH for review, but has not yet been reviewed, the applicant will be asked to withdraw either the pending application or the new one. Simultaneous submission of identical applications will not be allowed, nor will essentially identical applications be reviewed by different review committees. Therefore, an application cannot be submitted in response to this RFA which is essentially identical to one that has already been reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

H. LETTER OF INTENT

Prospective applicants are asked to submit by September 17, 1990 a letter of intent that includes a descriptive title of the proposed research, the name and address of the principal investigator, the names of other key personnel, the participating institutions, the number and title of the RFA in response to which the application is being submitted. Since taxol is in very limited supply, for planning purposes, the NCI requests the applicant to indicate the amount of drug that will be required to support the proposed studies.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information which it contains is extremely helpful in planning for the review of applications. It allows NCI staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent should be sent to:

BY US POSTAL

Dr. Matthew Suffness
Program Director
Grants and Contracts Operations Branch
Division of Cancer Treatment
National Cancer Institute
Executive Plaza North, Suite 832
Bethesda, MD 20892
Telephone: (301) 496-8783
FAX: (301) 496-8333

BY DIRECT DELIVERY

Dr. Matthew Suffness
Program Director
Grants and Contracts Operations Branch
Division of Cancer Treatment
National Cancer Institute
Executive Plaza North, Suite 832
6130 Executive Boulevard
Rockville, MD 20852
Telephone: (301) 496-8783
FAX: (301) 496-8333

I. INQUIRIES

Written or telephone inquiries concerning the objectives and scope of this RFA or inquiries about whether or not specific proposed research would be responsive are encouraged and should be directed to Dr. Matthew Suffness at the above address. The Program Director welcomes the opportunity to clarify any issues or questions from potential applicants.

Benefit Vs. Risk:

How FDA Approves New Drugs

by Dixie Farley

Under current law, all new drugs need proof that they are effective, as well as safe, before they can be approved for marketing. But it's important to realize that no drug is absolutely safe. There is always some risk of an adverse reaction. It's when the benefits outweigh the risks that FDA considers a drug safe enough to approve.

In fact, it was only 25 years ago that U.S. drug law first embraced the idea of risk vs. benefit that is now the key to new drug approval. Providing evidence of safety before marketing was first required by the Federal Food, Drug, and Cosmetic Act in 1938, but not until the Drug Amendments of 1962 did firms also have to show a drug's effectiveness before marketing. Before any drug gets on the market today, FDA decides—as quickly as a thorough evaluation allows—whether the studies submitted by the drug's sponsor (usually the manufacturer) show it to be safe *and effective* for its intended use. Here's what goes into those decisions.

"Take AZT, for example," says Robert Temple, M.D., director of FDA's Office of Drug Research and Review. (AZT stands for azidothymidine, the former name of the only approved AIDS drug, now known as zidovudine and marketed as Retrovir.) "An early look at a clinical study with the drug showed there were 19 deaths in patients taking a placebo [an inactive substance], but only one death in those on AZT. Unfortunately, AZT can cause serious adverse effects. Moreover, the drug is not a cure. The disease eventually progresses, despite treatment. We might not have approved the drug if we didn't also know that AZT was effective, that it prolongs life. As it was, an excellent study showed this."

Zidovudine was approved in March 1987 in a record 107 days. "No important new drug in recent memory has ever been acted upon so quickly," FDA Commissioner Frank E. Young, M.D., Ph.D., has said. But no corners were cut. Indeed, FDA expended an estimated eight staff years at a cost of $600,000 on zidovudine's evaluation. That the review was so rapid was due largely to the fact that FDA was involved with the drug every step along the way from the start of basic research. More than 4,000 patients received zidovudine during the course of its investigation. Thus, FDA reviewers were thoroughly familiar with zidovudine when its new drug application (NDA) was submitted. The drug approval process "at its best," Dr. Young calls that review. "But, no matter what we do," he says, "we want the public to know and understand that miracles don't happen overnight, that studies take years not months, and that patients are best served by rigorous testing and careful review."

◄

Every document on every shelf in this picture is part of a single new drug application—240 volumes in all. Looking up data in the application's medical section, which is so extensive it's housed in a storeroom rather than in the reviewer's office, is Dr. Alexander Fleming of FDA's division of metabolism and endocrine drug products.

PROMISING EXPERIMENTAL DRUGS

*I*n May 1987, FDA published a regulation to allow broader use of promising experimental drugs such as zidovudine so that desperately ill and dying patients can receive the benefits of those drugs years earlier than was possible before. *Promising* is the key word in this broadened use of unapproved drugs. FDA can't allow drugs to be used haphazardly. "It's a disservice," says FDA medical officer Alexander Fleming, M.D., "to let even a dying patient use an unproven drug unless qualified physicians believe it has some chance of helping. That only raises false expectations and might cause needless suffering or hasten death. A 'try anything' approach prevents physicians from quickly learning whether a drug works, and that's a disservice to others similarly ill who could be helped by an effective drug." In other words, FDA requires that experimental drugs, too, satisfy a certain benefit-to-risk ratio.

So, FDA reviewers scrutinize massive amounts of information in NDAs to evaluate the effectiveness and safety of new drugs. A drug is first reviewed, however, when a sponsor submits an investigational new drug application (IND) to FDA before tests with people begin. Within 30 days, FDA must let the sponsor know whether, in its judgment, the proposed test is sufficiently safe. If so, the IND is considered to be "in effect" and the clinical study may proceed; if not, FDA may place the study on hold until the sponsor makes needed changes.

Sponsors are encouraged to meet with FDA before the final phase of human tests, which are the large-scale controlled clinical trials. At this conference, FDA gives advice about the design of the sponsor's study plan to ensure that the trials will

(Continued on page 27)

A Drug Review Glossary

Abbreviated New Drug Application, or ANDA: A simplified submission permitted for a duplicate of an already approved drug. ANDAs are for products with the same or very closely related active ingredients, dosage form, strength, administration route, use, and labeling as a product that has already been shown to be safe and effective. An ANDA includes all the information on chemistry and manufacturing controls found in a new drug application (NDA), but does not have to include data from studies in animals and humans. It must, however, contain evidence that the duplicate drug is bioequivalent (see "Bioequivalence") to the previously approved drug.

Action Letter: An official communication from FDA to an NDA sponsor that informs of a decision by the agency. An *approval letter* allows commercial marketing of the product. An *approvable letter* lists minor issues to be resolved before approval can be given. A *not approvable letter* describes important deficiencies that preclude approval unless corrected.

Advisory Committee: A panel of outside experts convened periodically to advise FDA on safety and efficacy issues about drugs and other FDA-regulated products. FDA isn't bound to take committee recommendations, but usually does.

Amendment to an NDA: Submitted to change or add information to a not yet approved NDA or a supplement.

Bioavailability: Rate and extent to which a drug is absorbed or is otherwise available to the treatment site in the body.

Bioequivalence: Scientific basis on which generic and brand-name drugs are compared. To be considered bioequivalent, the bioavailability of two products must not differ significantly when the two products are given in studies at the same dosage under similar conditions. Some drugs, however, are intended to have a different absorption rate. FDA may consider a product bioequivalent to a second product with a different rate of absorption if the difference is noted in the labeling and doesn't affect the drug's safety or effectiveness or change the drug's effects in any medically significant way.

Clinical Studies: Clinical, or human, studies aim to distinguish a drug's effect from other influences—for example, a spontaneous change in disease progression or in the effect of a placebo (an inactive substance that looks like the test drug). Such studies conducted in this country must be under an approved IND (see "Investigational New Drug Application"), under the guidance of an institutional review board, and in accord with FDA rules on human studies and informed consent of participants.

Drug Product: The finished dosage form (tablet, capsule, etc.) that contains a drug substance, generally, but not necessarily, in association with other active or inactive ingredients.

Drug Substance: The active ingredient intended to diagnose, treat, cure, or prevent disease or affect the structure or function of the body, excluding other inactive substances used in the drug product.

Effectiveness: The desired measure of a drug's influence on a disease condition. Effectiveness must be proven by substantial evidence consisting of adequate and well-controlled investigations, including human studies by qualified experts, that prove the drug will have the effect claimed in its labeling.

Investigational New Drug Application, or IND: An application that a drug sponsor must submit to FDA before beginning tests of a new drug on humans. The IND contains the plan for the study and is supposed to give a complete picture of the drug, including its structural formula, animal test results, and manufacturing information.

New Drug: A drug first investigated or proposed for marketing after 1938 (when the Federal Food, Drug, and Cosmetic Act was passed)—that is, the drug was *not* generally recognized as safe and effective before that date.

New Drug Application, or NDA: An application requesting FDA approval to market a new drug for human use in interstate commerce. The application must contain, among other things, data from clinical studies needed for FDA review from specific technical viewpoints, including chemistry, pharmacology, medical, biopharmaceutics, statistics, and—for anti-infectives—microbiology.

Pharmacology: The science that deals with the effect of drugs on living organisms.

Post-Marketing Surveillance: FDA's ongoing safety monitoring of marketed drugs.

Pre-Clinical Studies: Studies that test a drug on animals and other nonhuman test systems. They must comply with FDA's good laboratory practices. Data about a drug's activities and effects in animals help establish boundaries for safe use of the drug in subsequent human testing (clinical studies). Also, because animals have a much shorter life span than humans, valuable information can be gained about a drug's possible toxic effects over an animal's life cycle and on offspring.

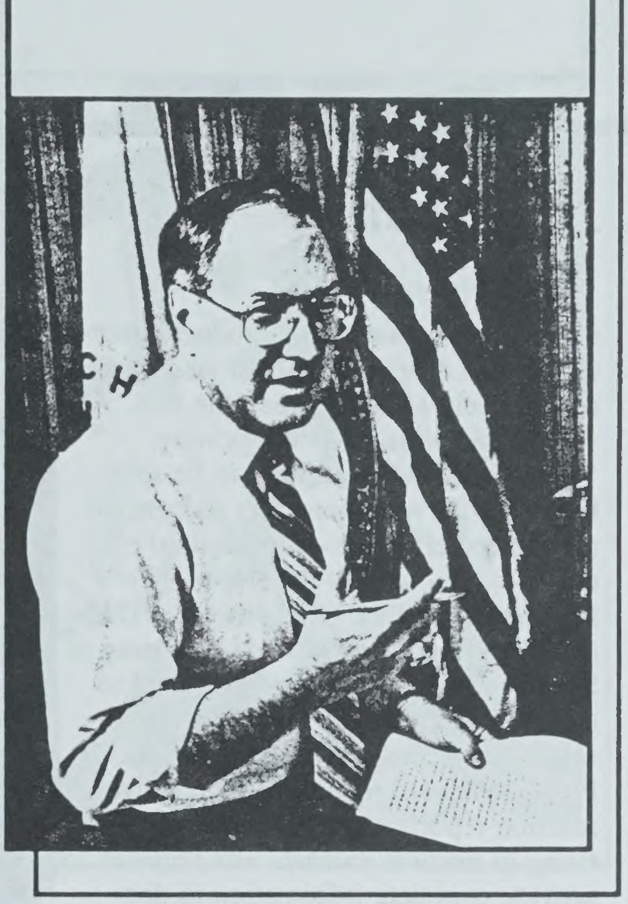
Raw Data: Researcher's records of patients, such as patient charts, hospital records, X-rays, and attending physician's notes. They may or may not accompany an NDA, but must be kept in the researcher's file. FDA may request their submission.

Review Clock: Time frame of 180 days allowed FDA to review NDAs. The "clock" starts on the date the NDA is received and stops the date a final action (see "Action Letters" entry) is taken. FDA may extend the time if significant changes are made to a pending NDA. From the time an NDA is submitted to when it's approved usually is more than 180 days, for any number of reasons—notably, time-consuming amendments or a shortage of trained reviewers.

Safety: No drug is completely safe or without the potential for side effects. Before a drug may be approved for marketing, the law requires the submission of results of tests adequate to show the drug is safe under the conditions of use in the proposed labeling. Thus, "safety" is determined case by case and reflects the drug's risk-vs.-benefit relationship.

Safety Update Reports: Reports that an NDA sponsor must submit to FDA about any new safety information that may affect the draft labeling statements about contraindications, warnings, precautions, and adverse reactions. Safety update reports are required four months after the application is submitted, after the applicant receives an approvable letter, and at other times upon FDA request.

Supplement: A marketing application submitted for changes in a product that already has an approved NDA. FDA must approve all important NDA changes (in packaging or ingredients, for instance) to ensure the conditions originally set for the product are not adversely affected. ■



Dr. Frank Young

(Continued from page 25)
be acceptable. As FDA's Temple puts it: "We have the experience of finding and eliminating flaws in the plan that we know will give us trouble later on in the NDA review. We don't want people to carry out a large study that has no chance of being considered adequate and well-controlled."

REVIEW TIME

*O*n the date FDA receives an NDA, a "review clock" is started; by law, FDA has 180 days to review the application and either approve or reject it. The span from "day 1" to "day of approval" is almost always longer than 180 days, however, both because the initial review takes longer than that and because it is usually necessary to carry out more than one review to resolve issues raised by the information initially submitted. Average approval time, in fact, is more like two years.

"So very often," says the drug center's Deputy Director Gerald Meyer, "we discover that we need more information. Sometimes, an applicant has it and can give it to us quickly. If not, a new study may need to be done and the data submitted. That stretches out the time before approval." But an application that doesn't have to be amended or resubmitted generally takes far less time to review, says Meyer—"an average of 10 to 18 months less time," in fact. Of the 926 NDAs approved from 1980 to 1986, 192 "got it right the first time" and, so, averaged just 13½ months. In 1987, in addition to the record 107-day approval time for zidovudine, the cholesterol-lowering drug lovastatin was approved in only nine months.

A REVIEWER'S DAY

*"I*f reviewers were doing nothing else, they could probably review an NDA in an outer limit of three months, maybe two," says Meyer. But that's not FDA reality, he is quick to point out. On many a day, a reviewer might be working with four NDAs, each consisting of numerous volumes of data, 12 equally voluminous applications for experimental drugs, and almost as many supplements to approved NDAs. Further, only about 60 percent of a reviewer's time is actually spent reviewing, Meyer says. The rest goes to attending hearings, answering inquiries, developing guidelines, purging trade secrets from documents requested under the Freedom of Information Act, and resolving such problems with drugs on the market as adverse reactions and faulty advertising.

Why is an NDA so lengthy? Because the documentation required is supposed to tell the drug's whole story, including: what happened during the clinical tests; how the drug is constituted—its components, composition, and toxicology; how it behaves in the body; and how it's manufactured, processed and packaged, especially the quality controls. FDA also requires samples of the drug and its labels.

Full reports of a drug's studies must be submitted because they are the basis of FDA's evaluation of safety and effectiveness. The controlled clinical trials are especially important because they involve the greatest number of patients. By providing for the appropriate comparisons to judge the drug's effectiveness and by revealing less common (even rare) side effects and adverse reactions, they help to clarify the drug's benefit-to-risk relationship. The final human studies also generate information that will be in the drug's professional labeling, the guidance approved by FDA on how to use the drug. This is the package insert that accompanies a drug in all shipments to physicians and pharmacies.

PRIORITIES

*T*he order in which applications are looked at is determined with the aid of a classification system. (See accompanying article.) As FDA resources are limited, the idea is to give priority to drugs with the greatest potential benefit. For example, AIDS drugs receive the highest priority, followed by drugs that offer a significant medical advance over existing therapies for any other disease.

Which of FDA's seven review divisions gets an NDA de-

(Continued on page 29)

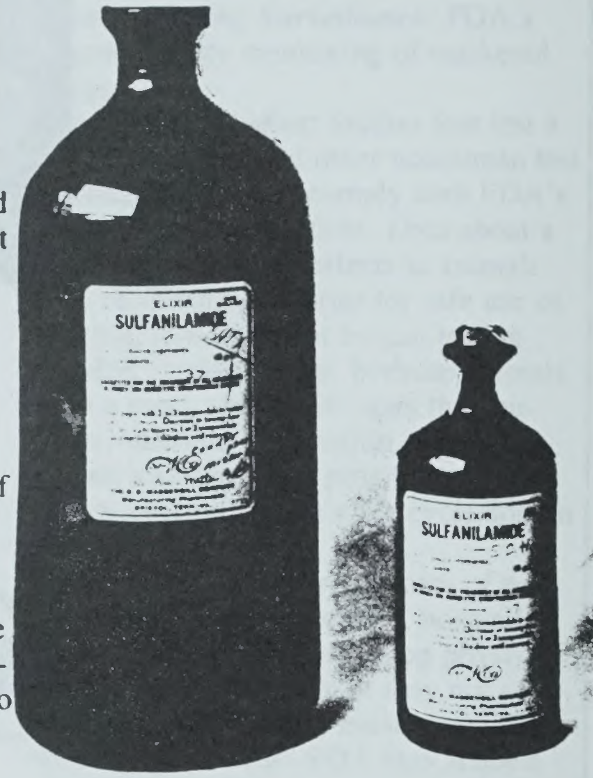
The Evolution of U.S. Drug Law

FDA acts as public health protector by ensuring that all drugs on the market are safe and effective. Authority to do this comes from the 1938 Federal Food, Drug, and Cosmetic Act, a law that has undergone many changes over the years, just as it changed earlier drug regulation. Some major milestones in the evolution of U.S. drug law are:

- ***Food and Drugs Act of 1906:*** This first drug law required only that drugs meet official standards of strength and purity. The burden of proof was on FDA to show that a drug's labeling was false and fraudulent before it could be taken off the market.
- ***Federal Food, Drug, and Cosmetic Act (1938):*** A bill was introduced into the Senate in 1933 to completely revise the 1906 drug law—widely recognized then as being obsolete. But Congressional action was stalled. It took a tragedy in which 107 people died from a poisonous ingredient in "Elixir Sulfanilamide" to prompt passage of revised legislation that, for the first time, required a manufacturer to prove the safety of a drug before it could be marketed. Among other provisions, the law also eliminated the Sherley Amendment requirement to prove intent to defraud in drug misbranding cases, provided for tolerances for unavoidable poisonous substances, authorized factory inspections, and added the remedy of court injunction to previous remedies of seizure and prosecution.
- ***Durham-Humphrey Amendment (1951):*** Until this law, there was no requirement that any drug be labeled for sale by prescription only. The amendment defined prescription drugs as those unsafe for self-medication and which should therefore be used only under a doctor's supervision.
- ***Drug Amendments of 1962:*** News reports about the role of FDA medical officer Frances O. Kelsey, M.D., in keeping the drug thalidomide off the U.S. market aroused public interest in drug regulation. Thalidomide had been associated with the birth of thousands of malformed babies in Western Europe. In October 1962, Congress passed these amendments to tighten control over drugs. Before marketing a drug, firms now had to prove not only safety, but also effectiveness for the product's intended use. The requirement was applied retroactively to 1938, when the FDC Act was passed. (Pre-1938 drugs were "grandfathered"—allowed to be sold because they were generally recognized as safe and effective—provided no evidence to the contrary developed.) To help implement the amendments, FDA contracted with the National Academy of Sciences/National Research Council to review the efficacy of drugs approved solely on the basis of safety since 1938. Firms were also required to send adverse reaction reports to FDA, and drug advertising in medical journals was required to provide complete information to doctors—the risks as well as the benefits.
- ***Orphan Drug Act (1983):*** "Orphans" are drugs and other products for treating rare diseases. They may offer little or no profit to the manufacturer, but may benefit people with the rare diseases. To foster orphan product development, this law allows drug companies to take tax deductions for about three-quarters of the cost of their clinical studies. Firms also are given exclusive marketing rights for seven years for any orphan products that are approved.
- ***Drug Price Competition and Patent Term Restoration Act of 1984:*** This law expands the number of drugs suitable for an abbreviated new drug application, or ANDA. ANDAs make it less costly and time-consuming for generics, which are often sold at lower prices than brand-name drugs, to reach the market. "Patent Term Restoration" refers to the 17 years of legal protection given a firm for each drug patent. Some of that time allowance is used while the drug goes through the approval process, so this law allows restoration of up to five years of lost patent time.

Though not involving changes in law, the following changes in FDA's drug regulations are noteworthy:

- ***Revision of New Drug Application Regulations (1985):*** These changes provide for safety reports after an application for a new drug is submitted, more focused and better organized data, use of summaries and tables for easier review, earlier problem solving, and allowance of approval on the basis of foreign studies alone. It also strengthens the monitoring of adverse reactions from marketed drugs.
- ***Revision of Investigational New Drug Application Regulations (1987):*** Encourages problem-solving meetings with FDA, requires deadlines in safety reports, and increases sponsor control over initial human test design so long as subjects face no unreasonable, significant risks.
- ***Treatment Use of Investigational New Drugs (1987):*** Patients with serious or immediately life-threatening diseases such as AIDS may now get treatment with experimental drugs that show reasonable evidence of potential benefit, provided no satisfactory approved therapy exists. This applies only to drugs already being studied in controlled clinical trials. Also, the drugs cannot expose patients to unreasonable risk. ■



The "Elixir Sulfanilamide" tragedy of 1937 ensured enactment the following year of the Federal Food, Drug, and Cosmetic Act. More than 100 people died from using the untested, poisonous new drug formulation, but FDA had legal authority to bring only a trivial charge of misbranding against the manufacturer. The product was labeled an "elixir," which implied it was an alcohol solution; actually, it was a diethylene glycol solution. If the term "solution" had been used instead, no charge of breaking the law could have been made.

Dr. Robert Temple

(Continued from page 27)

pends on the drug. Ulcer therapies, for example, go to the division of gastrointestinal and coagulation drug products; contraceptives go to the division of metabolism and endocrine drug products; and so on.

Each NDA comes in with a summary, usually less than 200 pages. Reviewers may spend several days reading through this and making notes to themselves, such as where to probe for further information and where the drug is likely to cause problems. Then, going through the studies one by one, reviewers ask such questions as:

- What is the study's design?
- Does it demonstrate what it's supposed to?
- Are the results of the studies reasonably consistent?

If the data are from a foreign country, FDA needs to know:

- Can FDA validate the data by an inspection or other means?
- Does the information apply to the American population and medical practice here? Medical practices, drug needs, and drug regulation vary from country to country, so drugs are often introduced in different countries at different times.

THE REVIEW TEAM

The members of the FDA review team simultaneously apply their special technical expertise to the review of an NDA:

- Chemists focus on how the drug is put together, whether the manufacturing controls and packaging are adequate to ensure the stability of the product, and whether the proposed labeling accurately reflects the effects of the drug.
- Pharmacologists evaluate the effects of the drug on laboratory animals in short-term and long-term studies.
- Physicians evaluate the results of the clinical tests—including the drug's adverse as well as therapeutic effects.
- Other staff evaluate the rate and extent to which the drug's active ingredient is made available to the body and the way it is distributed, metabolized and eliminated. They determine whether the evidence supports the labeling for the recommended dosing regimen. "The object is to give the patient no more drug than is absolutely necessary," says FDA's Meyer.
- Statisticians evaluate the designs for each controlled study, the validity of statistical analyses, and the conclusions of safety and effectiveness based on the study data.
- Microbiologists evaluate the data on anti-infectives (antibiotics, antivirals and antifungals). These drugs differ from others in that they're intended to affect the workings of microbes instead of patients. Reviewers need to know how the drug acts on these microorganisms, which ones it affects, any resistance to the drug, and clinical laboratory methods needed to evaluate the drug's effectiveness. Microbiologists also are concerned with determining whether injectable drugs can be made free of harmful organisms.

When an important new drug is about to be approved, a "Summary Basis for Approval" is written, laying out FDA's basis for deciding the drug is safe and effective. (Time may be saved if the sponsor drafts the summary for FDA's editing.) Each reviewer edits, or writes, the portion within his or her purview—chemistry, pharmacology, and so forth.

CONTACT WITH SPONSORS

Anytime during an NDA review, FDA may contact the sponsor or the investigators to discuss problems concerning the data. Indeed, FDA staff may visit the sites of some of the studies to compare results provided in the NDA with the physicians' patient records. If there are major deficiencies with any part of the NDA, substantially more work by the sponsor may be needed.

FDA frequently asks one of its 17 standing advisory committees on drugs and biologics (see p. 32) for advice. This is especially true when an approval decision is a "close call."

In the final analysis, FDA's decision whether to approve a new drug for marketing boils down to two questions:

- Do the results provide substantial evidence of effectiveness? This may be easy to figure out in a study with a drug to treat high blood pressure—if the drug works, the blood pressure goes down. But other studies, such as those testing a drug to treat depression, are more complicated.

(Continued on page 31)

Review Priorities

FDA classifies investigational new drug applications (INDs) and new drug applications (NDAs) to assign review priority on the basis of the drug's chemical type and potential benefit:

CHEMICAL TYPE

1. New molecular entity, or NME: An active ingredient that has never been marketed in this country. (Example: lovastatin, a drug approved in August 1987 to lower high blood cholesterol.)
2. New derivative: A chemical derived from an active ingredient already marketed (a "parent" drug). (Example: haloperidol decanoate, an injectable antipsychotic drug used to treat patients receiving prolonged treatment with injected tranquilizer drugs.)
3. New formulation: A new dosage form or new formulation of an active ingredient already on the market. (Example: estradiol as a controlled-release form of estrogen hormone administered via a skin patch.)
4. New combination: A drug that contains two or more compounds, the combination of which has not been marketed together in a product. (Example: human insulin isophane suspension/regular human insulin, an injectable semi-synthetic agent for regulating blood sugar.)
5. Already marketed drug product: A product that duplicates another firm's already marketed drug product: same active ingredient, formulation, or combination. (Example: another seller's version of meprobamate, a drug for treating depression.)
6. Already marketed drug product by the same firm: A new use for a drug product already marketed by the firm. (Example: minoxidil, a cardiovascular drug now being considered as a hair growth promoter.)

TREATMENT POTENTIAL

A. Important gain: May effectively treat or diagnose a disease not adequately treated or diagnosed by any marketed drug. Or, may improve treatment because it's more effective or safer. (Example: the cholesterol-lowering drug lovastatin.)
B. Modest gain: Offers a modest, but real, advantage over other marketed drugs—for example, greater patient convenience, elimination of an annoying but not dangerous adverse reaction, fewer required doses, or usefulness for special groups, such as for patients allergic to current drugs. (Example: norfloxacin, an antibacterial.)
C. Little or no gain: Essentially the same medical importance and use as a marketed drug. (Example: ketoprofen, an anti-inflammatory drug.)
H. Orphan drug candidate: Assigned orphan (see "Orphan Product" in glossary) status for purposes within FDA. (Example: clofazimine, a drug to treat leprosy, would have been in this class before it became "V," a designated orphan drug.)
V. Designated orphan drug: A drug for which the sponsor received orphan designation under the Orphan Drug Act. Such a sponsor is eligible for tax credits and exclusive marketing rights for the drug. (Example: clofazimine.)

Thus, a drug that is a new molecular entity and that represents an important therapeutic gain—such as lovastatin—is designated 1–A and receives the highest priority review, except for AIDS drugs. All drugs to treat AIDS (acquired immune deficiency syndrome) have been given top priority in a special class, "1–AA." ■

A Special System for OTC Drugs

FDA has always applied the same standards to nonprescription drugs as it does to prescription ones whenever proposed over-the-counter (OTC) products meet the criteria for "new drugs." (See "New Drug" in glossary.) In 1966, FDA contracted for a review of the effectiveness of all new drugs approved solely on the basis of their safety since passage of the 1938 Federal Food, Drug, and Cosmetic Act. Special attention soon became focused on OTC drugs: Of the 512 OTC drug products evaluated, 75 percent lacked substantial evidence of effectiveness.

That was when FDA decided it was time to tackle a broader review of OTC drugs—no small job, considering that more than 300,000 products were on the market. Those products, however, involved only about 700 active ingredients. It didn't take long for FDA planners to decide on a strategy: Classify the drugs by treatment category (antacids, laxatives, and so on) and evaluate the ingredients. So, rather than review thousands of, say, individual antacid products, FDA evaluated the far fewer active ingredients found in them—for example, aluminum hydroxide and magnesium carbonate.

That review, under FDA's division of OTC drug evaluation, is actually a three-phase process of producing a final regulation (called a monograph) to establish standards for each product-treatment category.

- The first phase, conducted from 1972 to 1981, was a review by panels of outside advisors who determined whether ingredients could be generally recognized as safe and effective for self-use. FDA published the reports in the *Federal Register*.
- The second phase—still continuing—is FDA's review of the panels' findings on the ingredients. In these reviews, FDA takes into account public comments and any new data. The conclusions are published as a proposed rule (or tentative final monograph).
- After considering any new information and objections, FDA publishes the final regulation, or monograph. Final rules have been published for 18 of the 81 product categories.

An OTC drug product doesn't need specific approval before marketing so long as it meets its category's standards.

Sometimes an approved prescription drug is deemed safe enough for self-use and is switched to OTC status. One-half percent hydrocortisone skin cream for temporary relief of minor skin irritation is an example.

A number of ingredients were taken off the market as a result of the advisory panels' OTC drug review. Among them were:

- Camphorated oil, a liniment often accidentally ingested with frequently toxic results.
- Hexachlorophene, once common in deodorant soaps, but now available only by prescription for special antimicrobial purposes because it may damage the central nervous system.
- Tribromsalan, removed from drugs and cosmetics because it was found to make skin extra sensitive to light.
- Zirconium, still safe in most forms of antiperspirants, but removed from aerosols because of concern it could cause lung nodules. ■

Gerald Meyer

(Continued from page 29)

- Do the results show the product is safe under the conditions of use in the proposed labeling? Reviewers note whether the adverse reactions show any disturbing pattern of occurrence. They "tease" out, so to speak, whether certain symptoms—such as headache or constipation—were caused by the drug or whether they occurred independently.

To be sure approval decisions reflect the most recent safety data, FDA requires safety updates four months after the NDA is submitted, again after it sends the firm an "approvable letter," and at other times as appropriate—before an advisory committee meeting, for instance. Updates must report new adverse reactions and important changes in the frequency or severity of effects that are known. Thus, new data suggesting that an adverse effect occurs more often than previously thought might change a "precaution" to a "warning" in the labeling.

FINAL ACTIONS

When FDA staff finish their evaluation, additional review is given by upper management. Final actions on nearly half of all NDAs are decided at the division level. The rest are approved or disapproved at the next management level of the drug center.

FDA then writes the applicant to say either that the drug is approved for marketing, is approvable provided minor changes are made, or is not approvable because of major problems. In the last case, the applicant can then amend or withdraw the NDA or ask for a hearing. Once its NDA is approved, a drug is on the market as soon as the firm gets its production and distribution systems going. FDA approves about 75 percent of all the NDAs submitted.

Most prescription and over-the-counter (OTC) drugs that were on the market before the Federal Food, Drug, and Cosmetic Act was passed in 1938 are "grandfathered." That means they are allowed on the market without the stringent proof of safety and effectiveness required of later drugs. Thus, FDA has not reviewed every single drug sold in the United States.

As new challenges arise, FDA drug review will no doubt continue to evolve. A vital part of that evolution, says Commissioner Young, is strengthening FDA's science base. A drug approval process "in which we can have confidence," he says, "requires scientific excellence as the basis for difficult regulatory decisions.... Recruitment is in full swing to build a corps of expert researcher-reviewers to improve our drug review program." Toward that end, FDA's staff of medical officers has increased in number by about 20 percent since 1985.

BIOTECHNOLOGY DRUGS

Further, FDA has approved several genetically engineered drugs, developed through the new science of biotechnology. Because reviewers work closely with sponsors and investigators during the drug development and testing stages, FDA has been able to review even such high-technology drugs in a timely fashion. Human insulin was approved first, in 1982. Since then, FDA has approved human growth hormone to treat children with pituitary gland deficiencies, two alpha interferons to treat a rare form of cancer, a monoclonal antibody to prevent kidney transplant rejection, and a hepatitis B vaccine.

The *way* reviewers look at data also is changing. Experimenting with NDAs submitted electronically, via computer, reviewers can retrieve, examine and reanalyze data from the drug's clinical trials. They can find out, for example, how many patients had any combination of signs and symptoms, provided that information was reported in the NDA. Reviewers need written reports to accompany the computer data, but the electronic NDA does promise to reduce paperwork substantially.

While change is inevitable and often desirable, there are some constants at FDA. Safety and effectiveness, risk vs. benefit, will remain the pivotal issues in FDA drug review. ■

Dixie Farley is a member of FDA's public affairs staff.

HAUSER

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FOR IMMEDIATE RELEASE
Boulder, Colorado
May 7, 1992

HAUSER CHEMICAL RESEARCH INCREASES TAXOL PRODUCTION CAPACITY TO 130 KILOGRAMS PER YEAR

Hauser Chemical Research, Inc. (NASDAQ: HAUS) announced the completion of process validation runs at its new production facility in Boulder, Colorado. Process validation is an important step in compliance with standard Food and Drug Administration (FDA) Good Manufacturing Practices (GMP) requirements. The plant has a production capacity of 100 kilograms of GMP taxol per year that can be fully achieved within 6 months and can be expanded when needed. According to the company's Chairman and Chief Executive Officer, Dean P. Stull, Ph.D., "Hauser's initial production facility is running at near capacity of 30 kilograms per year. The new facility will bring the company's total capacity to 130 kilograms per year."

Hauser is the only commercial supplier of bulk taxol for human use and has steadily improved the manufacturing process through technical innovation. As a result of these innovations, Hauser has reduced the Pacific yew bark needed to produce one kilogram of taxol to 16,000 pounds of bark. Hauser initially supplied bulk taxol to the National Cancer Institute for research purposes and currently manufactures bulk taxol, under a multi-year agreement, for Bristol-Myers Squibb Company which produces the final drug.

Hauser has also developed a method for the production of taxol from ornamental yew clippings which is similar to the current commercial process. Proving the new method on a pilot scale is under way. This could decrease significantly or eliminate the dependence on obtaining Pacific yew bark to support taxol production. The process for obtaining taxol from clippings will require FDA approval.

Taxol, an anti-cancer drug, is in clinical trials for refractory ovarian cancer, where it has achieved response rates up to 35%; and trials for breast cancer, where response rates of up to 50% have been achieved. The compound is also being studied widely in the treatment of other cancers. Bristol-Myers Squibb is expected to file a New Drug Application for taxol for ovarian cancer with the FDA by mid-1992.

Hauser Chemical Research, Inc. is a chemical processor, specializing in the extraction and purification of high value natural products using its proprietary technologies. Additionally, through Hauser Laboratories, the Company provides interdisciplinary laboratory testing services, chemical engineering services and contract research and development. The company is based in Boulder, Colorado.

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HAUSER

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President Hauser Northwest, Inc.
(303) 443-4662 (Colorado)

FOR IMMEDIATE RELEASE
Cottage Grove, Oregon/Boulder, Colorado
April 28, 1992

1992 BARK COLLECTION SEASON BEGINS; HAUSER PLANS TO EXCEED LAST YEAR'S COLLECTION OF 1,600,000 POUNDS

Cottage Grove, Oregon/Boulder, Colorado - Hauser Northwest, Inc. and its parent company, Hauser Chemical Research, Inc. (NASDAQ: HAUS), the only commercial producer of bulk taxol, announced today that the yew bark collection season has begun in the Pacific Northwest. Hauser Northwest plans to exceed last year's collection of 1,600,000 pounds of Pacific yew bark from public and private land. Hauser has imposed tough new standards on yew bark harvesters for the 1992 bark collection program. The new standards are designed to improve efficiency and tracking of the harvest process and are based upon knowledge gained from last year's harvest.

"April begins our third harvest season as the authorized collector of yew bark for taxol used in clinical trials," said Mike Trumbull, General Manager of Hauser Northwest. Hauser employs its proprietary extraction process to produce taxol for Bristol-Myers Squibb and the National Cancer Institute. "We are pleased with last year's accomplishments. We exceeded our harvest goals by salvaging bark from trees in clear cuts and established an environmentally sound program employing over 500 people. We are excited to begin the new season and to increase the availability of this important new drug."

Hauser Northwest has made significant improvements since last year in procedures, coordination, monitoring and data gathering. "As always, bark harvesters authorized by Hauser Northwest will hold valid permits from public agencies or private land owners. This year, we are using an improved set of trip tickets developed in cooperation with the Forest Service, BLM, private landowners and law enforcement personnel from a variety of agencies," said Trumbull. Trip tickets can be obtained only from authorized yew bark collectors, and every load of bark will be tagged with a highly visible, color-coded trip ticket.

Although the current source of taxol is Pacific yew bark, Hauser has completed a pilot process for production of taxol from the clippings of ornamental or nursery grown yew trees. Dependence on yew bark collected in the wild is expected to decrease as these alternative sources become available over the next 2 - 4 years. The company is also working with other researchers on methods of producing taxol in the laboratory.

Hauser Chemical Research, Inc., (the parent company of Hauser Northwest, Inc.) is a chemical processor, specializing in the extraction and purification of high value natural products using its proprietary technologies. Additionally, through Hauser Laboratories, the Company provides interdisciplinary laboratory testing services, chemical engineering services and contract research and development. The company is based in Boulder, Colorado.

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HAUSER

FOR IMMEDIATE RELEASE
Cottage Grove, Oregon [illegible]
April 24, 1992

1992 HARC COLLABORATION [illegible]
[illegible]

Cottage Grove, Oregon [illegible] ... Northwest [illegible] Pacific [illegible] ... improve efficiency and [illegible]

"[illegible] ... Cancer Institute. "We [illegible] ... at the availability of [illegible]

[illegible] ... tion, monitoring and data gathering. [illegible] Northwest will hold valid permits [illegible]

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Hauser Chemical Research, Inc., [illegible] ... cal processes, specializing in [illegible] ... ing on proprietary technologies. [illegible] ... provides [illegible] ... tract research and development. The company [illegible]

[illegible]

Appendix L

Cultural History of Pacific Yew

Appendix L

Cultural History *(Taxus brevifolia)*

Introduction

The Pacific yew has been a valuable though less frequently used tree of the Pacific Northwest since prehistoric times. Until recently, when taxol was extracted from the bark, the yew was primarily important for its wood, although bark and needles were used occasionally.

Yew trees normally grow widely scattered throughout the stands where they naturally occur. They are much smaller than the other conifers they grow with, and are generally much slower growing. These characteristics have kept yew from becoming a commercial species of great consequence. However, yew is currently harvested by boat builders, bowyers, and other woodworkers who are specifically seeking it out.

Native American Food Uses

Some British Columbia native groups (Haida at Masset) reported eating the flesh of the aril but warned that if women ate too many, sterility would result (Turner, 1982). Of the few tribes that ate them, there was general recognition that only small quantities should be eaten (Turner, 1982). Coast Salish people of the U.S. generally did not consider the yew to be a source of food. Many groups did dry, grind, or pulverize the needles for smoking. Most often this "tobacco" was mixed with kinnikinnick (a mixture of dried leaves and bark that was sometimes smoked by Native Americans and pioneers) or in later years with domestic tobacco (Gunther, 1973). The Karuk Tribe made use of the yew (and other tree species) for tobacco pipes (Davis and Hendryx, 1992).

Uses in Native American Technology

Yew was used by many northwestern Native American groups whenever a strong and tough wood was required. It was considered the premiere wood for construction of bows and other weapons from northern California to Canada and eastward to Montana (Davis and Hendryx, 1992; Gunther, 1973; Heizer, 1978; and Turner, 1979). Usually, the short bows were backed with elk sinew to provide extra strength. Extensive use was made of yew wood for harpoon shafts, spear shafts, arrows, canoe paddles, wedges, boxes, bowls, digging sticks, as well as knife and adz handles of the

highest quality. It was also used by some groups for canoe bailers, mat sewing needles, awls, net making, halibut and other fish hooks, canoe spreaders, bark scrapers, fire tongs, combs, and gambling sticks, drum frames, household utensils (especially spoons), and spring poles for deer traps. One group of interior Salish people felt it was the best material available for snowshoe frames (Davis and Hendryx, 1992; Gunther, 1973; Stewart, 1984; Turner, 1979).

In recent years Native Americans have used yew for shovel and ax handles. Native carvers still value yew highly but have had more difficulty finding large enough pieces for carving. The heartwood is strongly preferred for carving.

The Okanogan ground yew heartwood into a powder and mixed it with fish oil to make paint. Pacific yew was referred to as the "bow plant" or the "wedge plant" by several Native American groups (Turner, 1979).

Native American Medicinal Uses

The yew was traditionally used where strength was required and logically the tree was used medicinally to impart strength where it was needed. Smooth yew sticks were used by young Swinomish men to rub themselves to gain strength. The Swinomish also used boughs to rub themselves after bathing (Gunther, 1973). The Chehalis would crush yew foliage in a bath for old people and children to make them sweat and to improve their condition (Gunther, 1973).

The Klallam would also boil the foliage but drank the resulting infusion to cure internal injury or pain. The Cowlitz would grind moistened leaves and use the resulting pulp for a wound dressing. The Quinault reported chewing the foliage and spitting the pulp on wounds. While this reportedly stings, it promotes healing (Gunther, 1973).

The Quinault and Karuk tribes are the only groups that report using the bark which they peeled, dried, and then boiled, making a tea. The Quinaults drank the liquid as a lung medication (Gunther, 1973), while the Karuk used it as a stomachache relief and for kidney problems (Davis and Hendryx, 1992).

Native American Religious/Spiritual Values

In an ethnographic survey of the Mt. Baker-Snoqualmie National Forest in 1981, the authors describe the religious and spiritual views of the Coast Salish people who occupied the coastal areas of southwestern British Columbia, the Puget Sound trough, and down the coast (Suttles, Onat, and Hollenbeck, 1981).

The report contrasts the Judeo-Christian beliefs in a supernatural god who exists on a higher plane than humans and directs their lives. In contrast, the Coast Salish believed that they were simply part of a world of plants and animals. The Salish felt that they existed in this world on equal footing with these other species.

Native Americans typically sought out a "guardian spirit," "power," or "what he has" from the non-human part of the world which would help them in their lives. This power was most often gained through a spirit quest and in most cases was of value to the recipient in everyday life - the wolf might be of help to the deer hunter. A canoe carver might receive spirit help from the cedar tree from which he built a canoe or from the pileated woodpecker which also worked wood.

A significant point Suttles makes is that for the Coast Salish people, as well as many other Native American people, religion and spirituality were a part of everything they did. As indicated in the medical uses section, yew was used where strength was needed and it was also used where a strengthening of the spirit or power was required. It appears that yew may have been more important to Northwest Native Americans in the past than it is now:

- The Swinomish believed that they could receive power from the yew (Gunther, 1973).
- The Mount Baker-Snoqualmie inventory information suggests little current spiritual value although the Tullalip report decorating dancing shirts with small carved yew paddles (Suttles, Onat, and Hollenbeck, 1981).
- Whaling activity among the Makah was heavy with religious procedures. Though not practiced as it once was, whaling is a unique and important part of Makah culture (Waterman, 1920).

Uses in Contemporary Woodworking

Pacific yew wood is "even grained, very fine textured, heavy, very hard, very strong in bending and endwise compression, not stiff, very high in shock resistance, refractory to tools, finishes smoothly, [and is] very durable when exposed to conditions of decay" (Brown, 1949). Because of this scattered tree occurrence, commonly used logging systems and machinery are not practical for moving yew logs out of the woods. Harvest has required hand carrying logs or individually winching them out of the woods - the most inefficient ways of moving logs in today's production-oriented world.

Contemporary woodworkers have used yew wood in a fascinating number of ways. However, its scarcity and relatively small size limit its uses and applications. The current interest in harvesting yew bark could have a positive effect of making more yew wood available to woodworkers. Utilization of the wood would require loggers to work closely behind the bark peelers to move the logs out of the woods and protect them. The logs would have to be sealed on the ends and the logs stored in a shaded location; or the logs need to be sawn and the resulting billets or boards stickered and stored properly for air drying.

Turned Work

Pacific yew is currently used for a variety of items which are turned on a lathe. The wood is hard, dense, sands smoothly, and machines well. It is an excellent wood for turning spindles (bed posts, chair styles, tool handles and small spindles), bowls, and other vessels. Yew is occasionally turned for small specialty items, including the wooden parts of mechanical pen and pencil sets.

Furniture and Boxes

Yew is used in the construction of furniture of various kinds. Because it has become more difficult to obtain, it is now most often used for small accent pieces like wooden hinges, door and drawer pulls, and purely decorative features. It is used by northwest craftspeople for tables, chairs, bandsaw boxes, jewelry boxes, and accent features. Small pieces have also been used in marquetry.

Long Bows

A pamphlet from the Oregon State Forestry Department written over 40 years ago, before the advent of the modern fiberglass bows, says: "The western yew *(Taxus brevifolia)* is more in demand for archery stock than any other wood. The tree is quite widely distributed in the state but the best bows are made from wood that is grown in the higher elevations where the tree growth is slow and hence results in a close-grained product. Specifications for archery billets are as follows: They must be 3 feet 8 inches in length and 1 1/2 inches in thickness and 2 1/2 to 3 inches in width. Staves are 7 feet long with the same width and thickness as the billets" (Cronemiller, 1951). There are people who regularly cut a few trees for the construction of bows. Typically, bowyers harvest the wood from the forest, saw it into billets, and then season it, sometimes for decades.

Musical Instruments

Yew is used in the construction of a number of musical instruments, including flutes and recorders. The wood is also used for the parts of instruments; strips of yew have been used in the backs of lutes.

Boat building

Yew is an excellent wood for boat building, but its scarcity has limited the scope of its use. It steam bends well and is flexible and very rot-resistant. It has been used in wooden boats for steam-bent ribs, for knees, for breast hooks, and for edge grain decking. "Knees" and "breast hooks" on wooden boats were braces sawn from the natural bends in the tree where the grain would naturally curve and conform to the shape of the brace needed. These knees were much stronger than sawn braces (which cut across the grain) and simpler to fabricate than steam-bent braces (Wagner, 1985).

Carving and Sculpture

Yew carves beautifully and will take a fine polish from sharp carving knives. Its use is limited primarily by its scarcity and the small size of the material available.

Walking Sticks

A variety of walking sticks are made of yew. Canes have been constructed of a limb with a portion of the bole carved into a handle or hook. Hiking staffs have been made of limbs or carved out of the bole.

Architectural Applications

Specially selected pieces of yew have been used for house posts, railings, mantel timbers, and vertical-grain stair treads.

Landscaping Uses

Pacific yew generally does not compare well with English or other hybridized yews for landscaping. The foliage is generally more yellow-green and the trees and shrub forms have less visual character than other species. However, there are some local populations that have proven attractive to native plant fanciers and have been utilized in gardens.

As an Indicator Species

Although this use of yew relates to other species of *Taxus*, it illustrates the range of uses of this plant. Aldo Leopold *(naturalist and author of A Sand County Almanac)* was an avid hunter most of his life and eventually became an archer and bow maker. In the process of looking for yew with which to construct his bows, he observed many yew trees in forest environments, especially in his home state of Wisconsin and in German forests he visited on two occasions.

Leopold apparently first noticed the lack of yew in German forests where it had occurred. At the time the Germans were into high-production forestry as well as wanting their forests to produce lots of deer. When he questioned Germans about the lack of yew he was told that it had been all harvested and exported to England for long bows in historic times. Leopold knew that very few growing yew would yield wood of a quality for the construction of a long bow. After more questioning he concluded that the management emphasis on deer production had pushed ungulate populations beyond the habitat's capability to feed them. After

consuming the more palatable species, deer would begin to browse on conifers and in this case had consumed most of the yew in the country. In Leopold's home state of Wisconsin, there was a similar interest in managing as many deer as possible - to the detriment of the habitat (Flander, 1974; Leopold, 1953).

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Appendix M

Pacific Yew Research

Appendix M

Pacific Yew Research

Introduction

The amount of information we currently have about Pacific yew is relatively small, especially in comparison to that for other commercial forest tree species. For this reason, we include this appendix on needed research and current research projects in the Pacific Northwest involving Pacific yew.

Many of the research needs listed here were taken from "An Interim Guide to the Conservation and Management of Pacific yew." The projects listed under ongoing and future research projects are only those we are currently aware of.

Research Needs

Bark Harvest

1. Evaluate and compare the effects of yew bark harvest on:

    a. survival, growth, and reproduction;

    b. stand composition, structure, and density;

    c. gene flow and genetic variability;

    d. species response to environmental changes; and

    e. whole ecosystem health.

2. Determine optimal harvest levels that will maximize current taxol production with the fewest adverse effects.

Reproduction and Culture

1. Evaluate and compare Pacific yew reproduction in natural and nursery environments.

2. Determine how stump height, season of cutting, and shading affect stump-sprout genesis, survival, and culture.

3. Determine what mycorrhizal associates are needed for successful out-planting.

4. Determine what measures are needed to mitigate browse effects on seedlings.

5. Evaluate and study the following:

    a. the physiological factors and ecological conditions involved in asexual reproduction of Pacific yew;

b. the frequency, size, and distribution of seed crops;

c. the unique nature of sexual reproduction in Pacific yew, including male/female ratios in natural stands, and effective pollination distance;

d. seed dormancy and longevity data;

e. the optimal collection season and type of cutting, rooting media, hormone treatments, temperature, and moisture for large-scale production of rooted cuttings; and

f. proper outplanting techniques necessary for successful reforestation of Pacific yew.

6. Determine whether the germination capacity of yew seeds is altered when they are ingested by vertebrates, and identify which species of birds and mammals are responsible for yew seed dispersal.

Ecosystem Functions

1. Examine Pacific yew's specific role as an ecosystem component, and evaluate the following:

   a the effects of yew on the chemistry and biology of forest soils;

   b. herbivore associations with yew;

   c. the chemical and energetic quality of yew arils and foliage;

   d. the role of yew and its decay-resistant wood in creating microclimate and microhabitat conditions;

   e. relationships between Pacific yew and other plant and animal species;

   f. correlations between taxol production and environmental stress; and

   g. the effects of fire, predation (herbivore browsing and seed consumption), and competition from shrubs and overstory trees.

2. Determine what levels of yew harvest cause changes in the abundance or diversity of other vascular plants, vertebrates, invertebrates, fungi, and algae.

3. Determine how much yew could be harvested from streams without altering the physical, chemical, and biological attributes of those streams.

4. Determine the nutritional value of yew foliage, including the levels of anti-herbivory chemicals.

5. Evaluate the effects of removing yew from winter range areas.

6. Determine how crucial Pacific yew fruit is to the total food requirements of fruit-eating vertebrates and invertebrates in forest systems.

7. Identify whether removal of yew from spotted owl nest areas or home ranges alters the survival or reproductive fitness of spotted owls.

Timber Harvest

1. Evaluate the effects of timber harvest on Pacific yew survival, growth, and reproduction.

2. The following questions regarding Pacific yew and timber harvest should be answered:

    a. How do timber harvest and fragmentation affect Pacific yew and the populations of ungulates, fungal pathogens, and other organisms associated with yew?

    b. How is yew affected by broadcast burning?

    c. How is yew affected by soil compaction associated with mechanical slash piling?

    d. How does the sudden release associated with clearcutting affect understory yew? How severe is the damage, and what is its duration? How does this release affect yew survival, crown dimension, needle type and orientation, diameter growth, bark thickness, and foliage production?

    e. What are the effects of clearcuts-with-reserves, partial cuts, seed-tree, shelterwood, and selective-cut harvest systems, and how do they differ from the effects of conventional clearcutting?

    f. How do the various silvicultural systems influence stump sprouting, layering, seed production, seedling establishment, and browse production in Pacific yew?

Genetics

1. Identify population structures to provide mating-systems data, and separate genetic from environmental effects.

2. Determine the extent of genetic variation within and between yew populations.

3. Develop population viability models.

4. Determine the actual amount of genetic variability of Pacific yew.

Foliage Harvest

1. Foliage-harvesting methods should be evaluated, and compared in terms of their effects on yew survival, growth, and reproduction.

2. Determine the effects of foliage harvest on the following:

   a. stand composition, structure, and density;

   b. the local gene pool and gene exchange;

   c. evolution in response to changes in the environment; and

   d. the ecosystem.

Yew Inventory Data

In 1991 and 1992, the Pacific Northwest Region (R-6), USDA Forest Service conducted an extensive inventory of Pacific yew. The two primary reasons for the inventory were: 1. to characterize the current condition of yew, specifically by providing estimates of quantity and area distribution of yew; and 2. to characterize the existing vegetation on inventory plots to provide data for analyzing the relation of yew to existing vegetation.

The inventory was conducted by distributing sample plots systematically within the defined population. The population was also stratified using remotely sensed data. The population was restricted to National Forest System Land on seven National Forests in Oregon and Washington. The national forests included were: Siskiyou, Rogue River, Umpqua, Willamette, Mt. Hood, Gifford Pinchot, and the southern half of Mt. Baker-Snoqualmie.

Within these forests, the population was further restricted to a mid-level elevational zone. About 1800 field plots were established and measured. The primary sampling unit was a five-acre square plot. The five-acre plot was subsampled in several different ways to obtain data for a large number of different response variables.

The R-6 inventory resulted in a large data base on Pacific yew, a species for which very little information has previously been available. The inventory data represents a tremendous and valuable resource for expanding what is known about Pacific yew. A comprehensive plan for analyzing these data is being developed. This plan includes the following steps:

1. **Gather questions to be addressed** - Initially identify a large, exhaustive list of questions for which the database might provide information. Questions should include those by land/resource managers as well as research questions.

2. **Group questions into logical categories** - These groupings would be the beginning of identifying individual analytical studies to be conducted to completely analyze the database.

3. **Identify participants and their roles** - Identify the roles and responsibilities of the people who will be actually be involved in the analytical studies.

4. **Determine and secure resources needed to conduct studies** - The primary resources needed are funds and employees' time.

5. **Develop time frame** - Develop a time table for completion of the entire plan, including each identified analytical study. Studies should be carried out concurrently.

6. **Plan for publication** - Include a plan for comprehensive documentation of the results from the analytical studies.

Ongoing and Future Research Projects

A. Regeneration of Pacific Yew by Vegetative Propagation

Who is involved:

--Nan Vance, USDA Forest Service, Pacific Northwest Research Station, Corvallis, OR; and
--J. Herbert Stone Nursery, USDA Forest Service, Roque River National Forest, Central Point, OR.

Objectives:

- Determine optimization of rooting and growing procedures, growing environment, timing and sticking, rooting and lifting.

Time Frame: Winter 1990 to Spring 1993.

B. Using Protection Plants for Outplanted Pacific yew

Who is involved:

--Don Copes, Don Minore, Nan Vance, USDA Forest Service, Pacific Northwest Research Station, Corvallis, OR; and
--Bill Randall, USDA Forest Service, Siuslaw National Forest, Corvallis, OR.

Objectives:

- Determine if Pacifc yew stecklings inoculated with VA mycorrhizal will show greater growth and vigor than non-mycorrhizal stecklings.
- Determine if there is a difference in two species of *Glomus* (a VA mycorrhizal fungus) performance of Pacific yew stecklings.

Time Frame: Fall 1992 to Spring 1994.

C. Culture, Physiology, and Genetics Influencing Taxane yields

Who is involved:
--Rick Kelsey and Nan Vance, USDA Forest Service, Pacific Northwest Research Station, Corvallis, OR.

Objectives:

- Assess genetic variability of taxanes in Pacific yew across a broad geographic range.
- Determine variation in taxane concentration in different yew tissues and effect of light on taxane concentrations.
- Determine seasonal and diurnal effects on taxanes in foliage and bark of Pacific yew.
- Determine affect of nitrogen and light on growth and taxane concentrations of Pacific yew propagated by cuttings.

Time Frame: 1990 to 1993.

D. Pacific yew Regeneration by Seed

Who is involved:
--Nan Vance, USDA Forest Service, Pacific Northwest Research Station, Corvallis, OR.

Objectives:

- Develop procedures for handling, storing, and germinating Pacific yew seed.
- Understand dormancy and stratification requirements of seed.

Time Frame: Two or more years.

E. Distribution of Taxol in Bark of Pacific yew Trees

Who is involved:

--Rick Kelsey and Lorna Patterson, USDA Forest Service, Pacific Northwest Research Station, Corvallis, OR; and

--Department of Forest Science, Oregon State University, Corvallis, OR.

Objectives:

- Determine differences in taxol concentrations in the bark at different locations on bole and limbs.
- Develop a model to determine distribution of taxol in bark of bole and limbs and to more accurately determine bark mass on trees with simple field measurements.

Time Frame: 1992.

F. Assessing the Genetic Variability of Various yew Taxa

Who is involved:

--Alex Krupkin and Valerie Hipkins, Department of Forest Science, Oregon State University, Corvallis, OR.

Objectives:

- Assess techniques that would provide genetic markers.
- Analyze the genetic variability within and among yew species and assess genetic distance among taxa.

Time Frame: Study completed and manuscript in progress.

G. Factors Influencing the Reproductive Output of Pacific yew

Who is involved:

--Peyton Owston, Tom Spies, Nan Vance, Don Minore, and Leon Liegel, USDA Forest Service, Pacific North west Research Station, Corvallis, OR;

--Mark Wilson and Stephen deFazio, Department of Botany and Plant Pathology, Oregon State University, Corvallis, OR; and

--Gerald Krantz, Department of Enternology, Oregon State University, Corvallis, OR.

Objectives:

- Determine site and biological factors that influence seed production.
- Determine the importance of sexual reproduction in maintaining viable yew populations versus vegetative propagation.

Time Frame: 1992 to 1994.

H. Environmental Factors Affecting Growth of Pacific Yew Across the Northwest

Who is involved:

--Leon Liegel, USDA Forest Service, Pacific Northwest Research Station, Corvallis, OR.

Objectives:

- Identify site and/or stand factors associated with optimum yew growth.
- Characterize the landscape, understory, wildlife damage, and reproduction attributes of yew stands sampled within three physiographic provinces (dry, moist, and wet).
- Compare 80' to 100-year radial increment growth rate differences between yew trees of different diameters at the same site.

Time Frame: Summer 1992 to Summer 1993.

I. Genetic Improvement and Cultivation of Yew for Taxol

Who is Involved:

--Nick Wheeler , Keith Jeck, Sue Masters, Carol O' Brien, and Val Wyant, Weyerhaeuser Company, Rochester, WA.

Objectives:

- Estimate genetic parameters of taxane yield content.
- Determine the amount of variation in taxane yield.

Time Frame: Five-year study.

J. Partial Bark-Stripping of Pacific Yew

Who is Involved:

--Don Minore, USDA Forest Service, Pacific Northwest Research Station, Corvallis, OR.

Objectives:

- Relate partial removal of yew bark to subsequent tree vigor and growth.

Time Frame: 8 to 10 years.

K. Characterization of Pacific yew decline in a Northwestern Oregon Stand

Who is Involved:

--Catherine Parks, Art Tiedimann, Larry Bednar, USDA Forest Service, Pacific Northwest Research Station, La Grande, OR;
--Jerry Beatty, USDA Forest Service, Forest Pest Management, Portland, OR; and
--Edward Bottum, La Grande, OR.

Objectives:

- This is intended to be a pilot study to evaluate and document the condition of Pacific yew in a limited area, to assess damage and mortality (mostly due to bark stripping by elk), and inventory the study area for yew reproduction.

Time Frame: Spring 1993 and 1994.

L. Yew Ecology and Population Dynamics

Who is involved:

--Tom Spies, USDA Forest Service,
Pacific Northwest Research Station, Corvallis, OR.

Objectives:

- Evaluate the abundance of Pacific yew with respect to stand successional condition.
- Estimate population demographic characteristics of yew populations in natural stands.
- Develop population models to evaluate the effects of different levels of exploitation on the stability of wild populations of the species.

Time Frame:

M. Stump Sprouting of Pacific yew

Who is involved:

--Don Minore, USDA Forest Service,
Pacific Northwest Research Station, Corvallis, OR.

Objectives:

- Relate stump characteristics, season of cutting, and micro-environment to the initiation, growth, and survival of epicormic branches on Pacific yew stumps, so that successful asexual reproduction can be maximized in harvested yew stands.

Time Frame: Two or more years.

N. Soil Seed Banks in Pacific yew

Who is involved:

--Don Minore and Roger Ottmar, USDA Forest Service, Pacific Northwest Research Station, Corvallis, OR.

Objectives:

- Measure the occurrence and size of soil seed banks under representative female yew trees.
- Investigate conditions that promote the germination of dormant yew seeds (e.g. exposure to light, temperature, moisture, and fire).

Time Frame: 1993 and 1994.

O. Understanding the Physiology of Taxus Seeds for the Purpose of Developing Preservation protocols

Who is involved:

--Christina Vertucci, National Seed Storage Laboratory, Fort Collins, CO; and technical support, USDA Forest Service, Rocky Mountain Research Station, Fort Collins, CO.

Objectives:

- Determine seed sensitivity to desiccation at different stages of seed development and maturity.
- Assess seed viability and germination potential.
- Determine, where possible, those factors that contribute to deep embryo/seed dormancy.
- Test the efficacy of cryopreservation of germinable seeds.

Time Frame: Results will be reported in 1993.

Appendix N

Pacific Yew Harvest Policies

Appendix N

U.S. Forest Service and Bureau of Land Management Harvest Direction and Policies

This appendix contains policies, management direction and letters of guidance issued by the US Forest Service and the Bureau of Land Management, pertinent to the harvest of yew bark. They are arranged chronologically with the most recent directive presented first. Only directives issued at the Regional (Regions 1, 5 and 6) and Washington Office level have been included, with the Washington Office level appearing first. Forest level direction is generally more site-specific in nature and is directed towards on-the-ground implementation of individual harvest programs.

United States Department of Agriculture | Forest Service | Washington Office | 14th & Independence SW
P.O. Box 96090
Washington, DC 20090-6090

Reply to: 2470 **Date:** March 9, 1992

Subject: Pacific Yew

To: All Forest Service Employees

Research and clinical trials with taxol, extracted from the bark of Pacific yew, continue to show increasing promise as an anticancer drug. The National Cancer Institute has described taxol as the most promising anticancer agent discovered in the last decade. While our employees in Regions 1, 5, and 6 are most involved in the Pacific yew bark collection program, I want all employees to have an understanding of the Forest Service role in this program.

Virtually all Forest Service employees have been touched directly or indirectly by the death of a family member and/or a friend from cancer, and, indeed, the lives of all people in this country are likely to be affected by our dedication and commitment to the wise use of the Pacific yew resource. I want to commend our employees for their outstanding work in 1991. We implemented a very complex program in a very short period and our accomplishments exceeded our goals and expectations. This work, including conservation guidelines, inventory, research projects and an Environmental Impact Statement, will help ensure the Pacific yew resource is sustained for the future. The bark collected from National Forests in 1991 will produce enough taxol to treat more than 12,000 patients.

At the March 4, 1992, congressional hearing on Pacific yew, we learned that the next 2-4 years will be critical to the development of taxol. Without a continuous supply of Pacific yew bark, research, clinical trials, compassionate use, and patient treatment will be delayed. Alternative sources of the drug are being developed; however, they will not be available for human use for at least 2 more years and then only in small amounts until production can be increased.

Therefore, one of our most important tasks for the next 2-4 years is to continue our efforts to meet the need for Pacific yew bark. Pacific yew is one of the most important trees on the National Forests. All employees working in the Pacific yew ecosystems must be aware of the importance of this resource and take appropriate actions to ensure that the resource is effectively used. This will require close cooperation with our partners, a commitment and dedicated effort to know what is happening on the ground, and developing a personal knowledge of the program and its benefits to society.

I view this work as a significant example of caring for the resource and serving the people. I am proud that the Forest Service can play such an important role in developing a cure for cancer.

/s/ F. DALE ROBERTSON

F. DALE ROBERTSON
Chief

United States Department of Agriculture | Forest Service | Washington Office | 14th & Independence SW
P.O. Box 96090
Washington, DC 20090-6090

Reply to: 2430 **Date:** February 25, 1992

Subject: Commercial Sales - Pacific Yew

To: Regional Foresters, Regions 1, 5, and 6

The production of taxol as a cancer fighting agent continues to be an item of National interest and concern. The Forest Service must make sure that there is an opportunity to utilize as much Pacific yew as possible for the production of taxol. Presently, the Forest Products Lab is exploring methods to obtain taxol from Pacific yew heartwood. We must be sure that if a process becomes feasible that Pacific yew wood is not wasted or used for lower value products.

Therefore, I am directing you to take the following steps to assure that as much Pacific yew wood as possible will be available in the event that extraction of taxol from Pacific yew heartwood becomes feasible:

1. Do not sell Pacific yew wood for any use except research for taxol or minor miscellaneous uses (such as bows, arrows, and minor carving products).

2. Require removal of Pacific yew wood from all new timber sale contracts after bark removal. The wood must be transported to a secure location.

3. Require that Pacific yew wood be left in the forest or removed to a secure location on all bark collection permits

4. Maintain an inventory and location of all wood left in the forest.

There are some cutting units where logging is completed and Pacific yew bark has been removed but the Pacific yew wood has not been removed. It is not my intent to prohibit the burning of those types of units where burning is essential for reforestation.

Regions should develop procedures to accomplish the above until such time as a final decision is made whether this material can be used to extract taxol.

/s/ James C. Overbay (for)

F. DALE ROBERTSON
Chief

CONCURRENCE:R.Fitzgerald 02/21/92
Admin:S.Lang:02/24/92

United States Department of Agriculture | Forest Service | RO

Reply to: 2460 | Date: March 30, 1992

Subject: Interim Guidance for Harvest and Salvage of Pacific Yew

To: Forest Supervisors - NEZ, CLW, IPNF, KOOT,.FLT, Lolo NFs

This letter provides interim Regional direction for the management of Pacific yew and supplements current Regional guidelines. It provides direction and guidance for the following activities associated with managing and making yew available for the National cancer effort:

1. Harvesting bark within cutting units on existing and new sales.

2. Harvesting bark outside of existing or proposed cutting units.

3. Requirements for removal and storage of debarked yew wood.

4. Permitting of yew to parties other than Bristol-Myers Squibb (B-MS).

5. Post-harvest requirements for maintaining yew within timber sale harvest units in existing and new sales.

6. Analysis required for yew harvest operations.

7. Procedure for prioritizing harvest needs with B-MS collection agent, Hauser Northwest (Hauser).

To ensure that Hauser can meet your bark removal needs within a timely manner, we need to provide them with the following information:

1. A list of your top priority yew bark harvest areas, those that require the most immediate bark removal needs. This list should be provided as soon as possible and include those harvest units which contain bark from trees, stems, or slash that meet utilization standards that must be harvested prior to scheduled spring site prep and slash burns. Also include those logging units with pacific yew, that have not been logged, which you anticipate to be logged fairly early in the coming season. Please submit this list with a completed "Pacific Yew Harvest Estimates" form (enclosed) for each proposed activity.

2. Follow up by providing Hauser with a list of your second priority yew bark harvest areas. This list will include areas scheduled for fall burning or areas planned for logging later this summer or fall. Include other opportunities where the removal of yew is not urgent. Also accompany these lists with completed "Pacific Yew Harvest Estimates" forms. Note: Do not overlook other activities such as road construction, wildlife burns, etc. where usable yew may be lost.

Here are some general rules to help guide you in the decisions that need to be made for yew harvest and salvage program.

1. **Bark** - It is imperative that you make every effort reasonably practical to salvage yew bark containing usable quantities of taxol that could be lost in site preparation or burning activities. The following information will help you determine if the bark may still be usable.

   a. If the yew has been slashed in the past 12 months, the bark needs to be harvested. A stem, piece, or tree must have a minimum diameter of 3 inches on the butt or large end to be considered usable.

   b. If the yew was slashed 12 to 18 months ago, a sample of the bark needs to be sent to Hauser to see if the bark still contains usable amounts of taxol. To determine this, take bark samples from several useable size pieces and put them in a one-gallon zip lock bag (approximately 1 pound of bark) and ship it to:

      Hauser Northwest
      78120 Highway 99 South
      Cottage Grove, OR 97424

      If you want a quick turn-around, send via overnight priority mail. You will need to include a tag in the bark bag with your return address, phone number, date by which information is needed, where the sample was taken (District, Sale, Cutting Unit No.), and when the material was slashed. If you have a priority for need-to-know, Hauser can FAX you the results on the bark sample within 7 working days of receipt of material.

   c. If the yew was slashed over 18 months ago, it is not usable. Document the fact that the bark within the cutting unit was slashed too long ago to be usable as a source of taxol.

   New Sales - In all new sales bark should be harvested prior to logging. Any deviation from this direction would need to be a well-documented circumstance due to some unique timing problems. The purpose of this direction is to prevent loss of bark which can occur as a result of logging operations. Do not include Pacific yew as an included species in any timber sale contract and exclude yew from required slashing. Yew that is prescribed for leave should be protected with a reserve tree clause.

   Existing Sales - Where possible, schedule bark harvest before logging occurs. See Regional guidelines for direction. On sales that have been logged and that contain bark which meets the usability criteria, and this bark will be lost in site prep or burning activities, removal must be scheduled prior to site prep and burning.

Other Activities - If bark from stems or trees which meets the utilization standards is going to be lost as the result of other activities, the bark should be salvaged before those activities take place. Example - road construction or spring wildlife burns.

2. Wood - The heartwood of the yew contains a significant amount of taxol and may or may not be needed as a source of material for taxol in the future. Until it is determined that heartwood will not be a needed source for taxol, we will do the following on timber sales where yew wood will be lost in site preperation or other cultural activities:

   a. **New sales** - Bark will be stripped prior to logging. The stripped yew logs will be required to be decked in a designated area as part of the sales contract. An approved C Clause to accommodate this will be forthcoming. The minimum-size piece that will be required to be decked will be 8 feet in length with a small-end diameter of 4 inches or greater. The wood will be decked in a location where it will not be destroyed by site preparation activities and that does not provide open access to the public. The objective is to secure the material for future use. Records will be kept on the location of the decked material.

   b. **Existing Sales** - Where practical, yew wood will be salvaged before site preparation or burning; funding will be by activity that benefits from the burning or site prep. In some cases, circumstances, such as burning schedules, the unavailabilty of equipment, and minimal amounts of yew woood, may not permit us the opportunity to remove the yew wood. In making the decision on how to proceed, the amount of useable yew wood present should weigh heavily in the decision. It is not intended to prohibit burning of those types of units where burning is essential for reforestation or hazard reduction. Where opportunities exist, and time and funding are available, yew logs meeting the minimum specifications should be removed to a safe location.

   c. **Forest Product Permits** - Do not permit yew wood for any use other than for research for taxol or for minor miscellaneous uses (small quantities for traditional products such as bows and arrows or wood-carving projects). There will be no sales for such items as fence posts, lumber, etc., except as an option where the wood would be lost in site preparation activities where funding is not available to deck the material in a safe location for future possible taxol extraction.

   d. **Wood left from bark harvest taking place outside of Timber Sales** - the debarked wood will be left in the woods and the locations documented should the need arise for taxol production or, in the event of release, it might be used for other purposes.

3. **Post-Harvest Treatment** - The soon-to-be-released Conservation Biology Guidelines call for eventual yew stocking in the managed stand following harvest similar to pre-harvest conditions. We need to apply these guidelines to new and existing sales where we have utilizable size yew or yew having the potential of reaching utilizable size.

   a. **New Sales** - You need to meet the intent of the Conservation Biology Guidelines (which you will be receiving copies of by March 30). Silvicultural prescriptions shall address how we will achieve desired yew stocking in managed stands following harvest and the needed monitoring measures to ascertain if objectives have been met.

   b. **Existing Sales** - In harvest units with yew of utilizable size, where site preparation and burning activity have not taken place, you need to modify site preparation and burning to favor yew in the managed stand following harvest. If site conditions will not permit you to modify prescriptions to the extent needed to meet the intent of the Conservation Biology Guidelines (an eventual stocking similar to pre-harvest conditions), you need to plan for planting yew to supplement the expected shortfall in yew stocking in the managed stand. We need to document pre-harvest levels of yew stocking and conduct surveys following burning that will compare post-treatment levels with pre-harvest levels for yew stocking. Keep in mind that sometimes the roots or stumps do not sprout for 1-2 years following a burn, so failure to resprout promptly does not indicate that the stump is dead. The CDA Nursery has conducted trials on propagation of yew from seed and rooted cuttings and have had excellent success with rooted cuttings. They will be a source of planting stock for yew in the future. Note: There is information becoming available regarding successful natural regeneration of yew while meeting site prep and hazard reduction objectives. This should be reviewed by personnel involved in making silviculture and fire prescriptions.

4. **Environmental Analysis** - On any proposed projects that have the potential of affecting utilizable-size yew, or yew which has the capability of reaching a utilizable size, we have to address the effects of the proposed action on the yew. Projects which could affect yew populations would include timber harvest, road construction, wildlife burns, and any other vegetative-disturbing projects where yew populations occur. Analyses should also address the salvage of yew for use in the production of taxol in those projects where yew of utilizable size will be lost in implementing the activity. For timber harvest projects, alternatives need to meet the intent of the Conservation Biology Guidelines. Any alternative that departs from the Conservation Biology Guidelines needs to display the departure rationale. This also holds true for yew harvest permits outside of timber harvest areas. Modifications of existing sales that are made to meet the intent of the Conservation Biology Guidelines will not need a new decision notice, if they do not significantly alter the intent of the original decision. However, documentation of the analysis leading to the decision to modify silvicultural prescriptions to comply with the Conservation Biology Guidelines will be kept in the project file and key publics informed of the decision.

Projects where yew is being salvaged due to other activities will not require an environmental analysis, if removal of yew has been addressed by the parent document. However, yew harvest proposals outside of existing project areas will need an environmental analysis. That analysis shall address the Conservation Biology Guidelines and the effects of the proposed yew harvest on other resources. A programmatic EIS for yew harvest is presently being written but it will not be completed in time to cover the 1992 harvest season.

A Pacific Yew Pre-harvest Estimate form is enclosed. Use this form when requesting Hauser to harvest yew. This form will provide the consistency in information and data that Districts and Hauser need to prioritize harvest requests and develop harvest schedules.

/s/ JOHN M. HUGHES
for

DAVID F. JOLLY
Regional Forester

Enclosures

M.DAVIS:md:mek:3/16/92
I **CONCUR:M.DAVIS:03/16/92I CONCUR:D.FOTH:03/26/92CONCURRENCE:D.SPORES: 03/26/92**

TREE DIAMETER, HEIGHT, POUNDAGE ESTIMATE

Diameter	*Height	Pounuages (Green)
3"	1/2	2 - 5
4"	1/2 to 1	4 - 8
6"	1 to 1/2	8 - 14
8"	1 to 1-1/2	14 - 25
10"	1 to 1-1/2	30 - 40
12"	1 to 1-1/2	30 - 50
14"	1-1/2 to 2	40 - 60
16"	1-1/2 to 2	50 - 80
18"	2 to 2-1/2	70 - 100
20"	2-1/2 to 3	80 - 120
24"	2-1/2 to 3	100 - 140
28"	3 to 3-1/2	100 - 160

*Based on 16' Log Length

Note: These are average poundages. Due to the shape and irregularity from one yew tree to another, there can be large differences in poundages.

estimate(kordon)wp

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ECØFOREST SERVICE
ECØPACIFIC YEW PRE-HARVEST ESTIMATE

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Forest ______________________________
District ______________________________
Date ______________________________

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Permit# ______ Name _________ TS Name ________________________________ Unit# _____

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Acres _________ Aspect ________ Elevation ________ Legal Description _________________

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Re-Harvest (yew)

No$X

Yes$X

(See notes below)

Pre Harvest No$X

Yes$X

Mo/Yr to begin logging ______________________________

Post Harvest No$X

Yes$X

Mo/Yr logging completed ______ Mo/Yr to burn _______

Yew Harvest Only

No$X

Yes$X

Mo/Yr to begin harvesting _______

T

T

CTL

C2L

C3L

C4L

ECCCT.S. Contract

No$X

Yes$X

Purchaser____

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ECCCEstimated Quantity (Diameters measured at top of stump)

T

C2L

C3L

C4L

C5L

No. Live Trees	3-8"______	9-15"______	16"+______
No. Dead Trees	3-8"______	9-15"______	16"+______
Est. Pounds	3-8"______	9-15"______	16"+______

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Total Pounds ___________

N

ECCCType of Harvest Activity

T

C2L

C3L

Hand Peel _______ ECCO(% of unit)

Pick-up with Winch _______ ECCO(% of unit)

Cable Yarding _______ ECCO(% of unit)

Other (describe) _______

T

DDD

ECCCAdditional Comments: ECCO(Scattered, clumped, or spread evenly throughout area, location of concentrations.)

RX9

Notes:

*Re-harvest (yew) includes units that have previously been harvested for yew, but additional yew must be removed. If unit must be reharvested, check whether the unit is pre T.S., post T.S., or yew harvest only.

*Pre-harvest includes units scheduled for clearcut, partial cut or other silvicultural treatment where yew bark collection must be completed before other activities begin.

*Post-harvest includes units where logging activity has taken place and yew bark collection must be completed before burning or other silvicultural treatments can begin.

*Yew harvest only includes units scheduled for harvesting outside clearcut or partial cut areas.

*Please attach a sale area map or copy of TRI card.

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EC©© _______________ NATIONAL FOREST
EC©© _______________ RANGER DISTRICT

EC©©ADMINISTRATIVE USE PERMIT - YEW HARVEST
EC6Ref: 36 CFR 223.2(C),

Permit # _________

Permission is hereby granted:	Hauser Northwest, Inc. Acting as an Agent for Bristol Myers-Squibb 78120 Highway 99 South Cottage Grove, OR 97424	Trip Ticket # ___________ Date Issued: ___________ Termination Date: ________ Extended to: ___________

Represented by:

_______________ & _______________

Agent's Representative — Field Supervisor

Ph: ____________ Ph: ____________

DBTHE PURPOSE for this transfer is to harvest and remove bark and other parts from Pacific yew (Taxus brevifolia) from the National Forest lands described below. The transfer of Pacific yew is provided for in THE COOPERATIVE AGREEMENT between BRISTOL-MYERS SQUIBB, CO., and USDA FOREST SERVICE, dated 6/19/91. This transfer is subject to all the terms and conditions of the Cooperative Agreement, all subsequent amendments, and the ANNUAL PACIFIC YEW PROGRAM PLAN and to the provisions attached hereto.

DDDDESCRIPTION OF PACIFIC YEW PERMITTED (Specify product; estimated bark weight, or measure of other products. Identify means of designation. Include or refer to any special cutting or harvesting prescriptions.)

UTILIZATION SPECIFICATIONS: Unless specified below, all stems with a large end or stump diameter of 3" or larger shall have all bark from stems and branches down to a 1 inch small end diameter removed from the Permit Area and delivered to the agreed upon Delivery Point.

DESCRIPTION OF LANDS FROM WHICH PACIFIC YEW WILL BE TAKEN (Include legal description of area. Include map of the location, name and extent of area(s).

Delivery Point: ____________ Haul Route by Road Numbers: ________________

In consideration of such permission I agree to -

1. Harvest only such Pacific yew as is designated by a Forest Officer.
2. Remove no Pacific yew product until permission is given.
3. Conduct the harvesting and dispose of the refuse as directed by the Forest Officer.
4. Comply with the TERMS and CONDITIONS listed in all attachments to this Permit.
5. Comply with all other regulations governing National Forests.
6. Conduct operations in a workmanlike and orderly manner, with a timely completion of any harvest area entered.

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I understand and agree that cutting or taking any material under this Permit makes all the conditions binding. I further understand that the Code of

Federal Regulations, Part 261, pertain to this Permit and that violations of this Permit may be prosecuted thereunder.

Accepted by: ______________________________ Date: ____________
Designated Agent/Representative

Approved by: ______________________________ Date: ____________
Authorized Forest Officer

(5/5/92)
ATTACHMENT 2 1992 Annual Pacific Yew Program Plan

Utilization Standards for Harvest of Pacific Yew Bark.

The utilization of Pacific yew bark has two parameters: 1) the minimum size of material to be peeled, and 2) an established minimum amount of bark to be stripped from the trees in an area designated for peeling.

1) Unless otherwise provided for in a yew harvest prescription that designates certain yew to be left, yew bark should be harvested from pieces and stems which have a large end or top-of-stump diameter of at least 3 inches. On such pieces, the bark should be removed to a 1-inch small end diameter at the top of the stem and branches.

2) Any stem or portion of tree which is to be utilized for bark that can meet the wood utilzation storage standards of being eight feet in length to a small end diameter of 4 inches will not be bucked below the 4 inch top unless bucking can be done in multiples of eight feet or longer.

3) The goal is to collect all of the yew bark feasible from trees designated for harvest. Realistically, on-the-ground, a collection of 95 percent is a practical goal. The other 5 percent could include bark in flutes, some trees that are unpeelable due to seized bark caused by damage or other factors, and an occasional tree that may not be found.

There are instances where a few trees are located in difficult to reach areas or far away from general collection area. Decisions as to whether or not this bark would be collected will be made by the local District Coordinators on a case-by-case basis.

5/5/92
ATTACHMENT 3

STANDARD PROVISIONS
TO ADMINISTRATIVE USE PERMITS

STANDARD CONDITIONS

1. Transfer of Title - Title of all Pacific yew products included in this permit shall remain in the United States until it has been harvested; counted, measured or weighed; and leaves the National Forest.

2. Measuring of Products - Bark is to be field weighed prior to removal from the Permit Area using scales approved by the Forest Service; other products are to be counted, measured or tallied in a manner approved by the Forest Service prior to removal from permit area.

3. Authorization - Any individual, while harvesting, transporting or otherwise handling Pacific yew under the terms of this permit shall have a document in their possession authorizing them to do so; or be under the immediate supervision of an individual who posesses such an authorization, is delegated supervisory authority, and is present in the immediate area of the activity.

4. Pacific Yew Removal Receipts: Any individual harvesting, transporting or otherwise handling Pacific yew under the terms of this permit shall utilize the five part serially-numbered Pacific Yew Trip Ticket for the transportation and accounting of the yew harvested by this permit.

--Part E shall be used as a haul permit, shall contain a field a measurement of the quantity removed and will be displayed at the back of the load.

--Part A shall contain a field measurement of the quantity removed will be returned to the Forest Service office from which it was issued or deposited at a location designated by the Authorized Officer.

--Part B contain both the field measurement of the quantity removed and the certified measurment of the product as recorded into the inventory of the agent and will be returned to the Forest Service office from which it was issued.
--Parts C and D are agents reciepts for inventory management.

If and when the Pacific Yew Trip Ticket are not available, serially-numbered Forest Products Removal Receipts may be used.

The Forest Products Removal Receipts shall contain:

1. Product description (bark, bole, needles, etc.);
2. Quantity being removed, (bark by field weight, other products by a method of measurement approved by the Forest Service;
3. Unit of measure (pound, lineal foot, number, etc.)
4. Permit number;
5. Issuing Forest Service office;
6. Name and original signature of Field Supervisor.
7. Date and time of removal from Permit Area;
8. Haul vehicle description;
9. Haul vehicle license number;
10. Gross weight; and,
11. Name of Harvestor.

5. Conduct of Operations - B-MS shall conduct all operations under this permit in a safe, workmanlike manner, and shall minimize soil erosion and damage to young growth or trees left standing, and take all reasonable precautions to prevent pollution of air, soil, and water.

Tree stumps shall be cut not to exceed 14 inches or less than 12 inches with bark intact to promote sprouting. On brush form yew that has a portion of the stem trailing below ground level, the stems can be cut as near flush with ground level as possible and shall not exceed 14 inches. Brush form yew that does not have a portion of the stem trailing below ground level will be cut to leave at least a 12 inch stem with bark intact and shall not exceed 14 inches.

When skidding or yarding are required to remove slashed stems to facilitate peeling, the area of permitted skidding or yarding will be shown on the Permit Area map. Skidding and yarding equipment to be used will be approved in writing for those areas specified on the permit.

Unless shown on a Permit Area Map, mechanized skidding or yarding equipment is prohibited unless otherwise agreed to in writing.

Unless otherwise agreed to in writing, transportation of Pacific yew harvested under this permit will occur only on the haul route identified as identified on the Permit Area Map.

Unless otherwise agreed to in writing, harvesting and transporting of Pacific yew will be confined to daylight hours.

6. Harvest of Yew in Riparian Areas - Riparian Areas which are subject to this Provision are shown on a Permit Area map. Unless otherwise agreed, the harvest of yew will not take place within 75 feet from stream courses within riparian areas.

7. Use of Premises, Camps - Before any camp is set up on lands administered by USDA Forest Service, B-MS or their Agent shall obtain written permission through the District Ranger. A camp is interpreted to include a campsite or trailer parking area of any individual working on this permit for B-MS.

8. Conduct of harvesting Critical Multiple-Use Areas - In areas designated as "Modified Logging Area" on a Permit Area Map, the following measures are applicable unless other methods or requirements are agreed to in writing between B-MS and Forest Service.

(a) Nonspecified roads, skid roads and landings shall be located on the ground and approved by Forest Service prior to construction or the felling of adjacent timber.

(b) Felled or windthrown timber that must be disturbed in construction of roads, skid roads or landings shall be bucked prior to moving if necessary to minimize disturbance to forest values.

(c) Trees shall be felled and skidded in such a manner as to minimize disturbance to surrounding forest values.

(d) Limbs that may do damage to forest values shall be severed prior to skidding.

(e) Use of tractors shall be restricted to skid roads and other approved cleared areas.

(f) Landing size will be held to a minimum.

(g) Skidding shall be away from existing roads, trails, water sources, streamcourses and occupancy areas.

9. Protection, Use and Maintenance of Improvements - B-MS, in all phases of harvest operations, shall protect, insofar as practicable, all land survey corners, telephone lines, ditches, fences and other improvements. If such improvements are damaged by B-MS's operations under this permit, B-MS shall restore them immediately to condition existing immediately prior to damage. All roads and trails designated by Forest Service as needed for fire protection or other purposes, shall at all times be kept free of logs, brush, and debris resulting from B-MS's operations. Roads or trails damaged shall promptly be restored by B-MS.

B-MS use of existing roads may be restricted when indicated on a Permit Area map.

10. Streamcourse Protection - Streamcourses which are subject to this Provision are shown on a Permit Area map. Unless otherwise agreed, the following measures shall be observed to protect streamcourses.

(a) Operations shall be conducted to prevent debris from entering streamcourse. In event B-MS operation causes debris to enter streamcourses in amount which may adversely affect the natural flow of the stream, water quality or fishery resource, B-MS shall remove such debris as soon as practicable, but not to exceed 48 hours, and in an agreed manner that will cause the least disturbance to streamcourses.

(b) Culverts or bridges shall be required on temporary roads at all points where it is necessary to cross streamcourses with mechanized equipment. Such facilities shall be of sufficient size and design and installed in a manner to provide unobstructed flow of water and to minimize damage to streamcourses. Trees or products shall not be otherwise hauled or yarded across streamcourses unless fully suspended.

(c) Wheeled or track-laying equipment shall not be operated in streamcourses except at crossings designated by Forest Service or as essential to construction or removal of culverts and bridges.

11. <u>Landings, Roads, and Skid Trails</u> - Landings, roads and skid trails to be used shall be agreed upon prior to their use; and improvements on existing facilities shall not exceed that needed for safe and efficient operations.

Slash, stumps or other debris resulting from improvement of facilities shall be treated or disposed of as slash unless agreed otherwise.

After landings have served B-MS's purpose, B-MS shall ditch or slope them to permit water to drain or spread. Unless agreed otherwise, cut and fill banks around landings shall be sloped to remove overhangs and otherwise minimize erosion.

After a temporary road or skid trail has served B-MS's purpose, B-MS shall remove bridges and culverts, eliminate ditches, outslope roadbed, remove ruts and berms, effectively block the road to normal vehicular traffic where feasible under existing terrain conditions and build cross ditches and water bars as staked or otherwise marked on the ground by Forest Service. When bridges and culverts are removed, associated fills shall also be removed to the extent necessary to permit normal maximum flow of water.

12. <u>Protection of Cultural Resources</u> Location of known historic or prehistoric sites, buildings, objects, and properties related to American history, architecture, archaeology and culture, such as settler or Indian artifacts, protected by American Antiquities Act of 1906 (16 U.S.C. 431-433), yational Historic Preservation Act of 1966 (16 U.S.C. 470) and the Archaeological Resources Protection Act of 1979 (PL 96-95 and 36 CFR 261.9(e)) shall be identified on the ground by Forest Service. Forest Service may unilaterally modify or cancel this contract to protect an area, object of antiquity, artifact, or similar object which is or may be entitled to protection under these Acts regardless of when the area, object or artifact is discovered or identified. Discovery of such areas or objects by either party shall be promptly reported to the other party.

In the event of contract modification under this Subsection, B-MS shall be reimbursed for any additional protection required, provided that any work or extra protection required shall be subject to prior approval by Forest Service. Amount of reimbursement shall be determined by Forest Service and shall be in the form of a reduction in stumpage rates unless agreed otherwise in writing. However, in no event may stumpage rates be reduced below base rates. B-MS shall protect <> all known and identified historic or prehistoric sites, buildings, objects and properties related to American history, architecture, archaeology and culture against destruction, obliteration, removal or damage during B-MS's operations. In accordance with 36 CFR 296.14(c), B-MS shall bear costs of restoration, provided that such payment shall not relieve B-MS from civil or criminal remedies otherwise provided by law.

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Wheeled or track-laying equipment shall not be operated within such areas except on roads, landings, tractor roads or skid trails approved under SP12. Unless agreed otherwise, trees will not be felled into such areas. B-MS may be required to backblade skidtrails and other ground disturbed by B-MS's operations within such areas in lieu of cross ditching required under SP10.

13. Use of Timber - This permit is subject to the Forest Resources Conservation and Shortage Relief Act of 1990 (101 Stat. 714-726; 16 U.S.C. 620 et. seq.).

Except for species determined pursuant to public hearing to be surplus, unprocessed Pacific yew meeting the minimum specifications identified in Clause 9 below shall not be exported from the United States nor used in direct or indirect substitution for unprocessed timber exported from private lands by B-MS or any person as defined in Section 493 (16 U.S.C. 620e) of the Act.

Timber in the following form will be considered unprocessed: (a) trees or portions of trees or other roundwood not processed to standards and specifications suitable for end product use; (b) lumber, construction timbers or cants, intended for remanufacturing, not meeting standards defined in Section 493 (16 U.S.C 620e) of the Act; and (c) Aspen or other pulpwood bolts exceeding 100 inches in length.

Unless otherwise agreed in writing, unprocessed Included Timber shall be delivered to a domestic processing facility and shall not be mixed with logs intended for export.

Prior to transfer, during the life of this permit, and for a period of 6 years from Termination Date, B-MS shall furnish to Forest Service upon request records showing the volume and geographic origin of unprocessed timber from private lands exported, or sold for export, by B-MS or affiliates.

Prior to delivering unprocessed Included Timber to another party, B-MS shall require each buyer, exchangee, or recipient to execute an acceptable agreement, which shall: (1) identify the federal origin of the timber, (2) specify domestic processing for the timber involved, (3) require the execution of such agreements between the parties to any subsequent transactions involving said timber, (4) require that all hammer brands and/or yellow paint must remain on logs until they are either legally exported or domestically processed, whichever is applicable, and (5) otherwise comply with the requirements of Section 492 (16 U.S.C. 620d) of the Act.

No later than 10 days following the execution of any such agreement between B-MS and another party, B-MS shall furnish to Forest Service a copy of each such agreement. B-MS shall retain, for 6 years from Termination Date, the records of all sales, exchanges, or dispositions of all Included Timber.

For breach of this provision, Forest Service may terminate this permit and take such other action as may be provided by statute or regulation, including the imposition of penalties. When terminated by Forest Service under this provision Forest Service will not be liable for any claim submitted by B-MS relating to the termination.

14. Product Identification - Unless Forest Service determines that circumstances warrant a written waiver or adjustment, (1) all Pacific yew logs that meets minimum standards of an 8 foot piece with a minimum 4 inch small end diameter shall be hammer branded on both ends with an assigned brand, (2) all domestic processing products shall be painted on both ends with highway yellow paint. B-MS will furnish and apply highway yellow paint of a lasting quality

(oil base or equivalent). Paint sticks are not acceptable. Each paint mark must cover an area equal to a 2-inch circle.

All log or trees shall be branded with the assigned sale brand before removal from permit area. Such brands shall be State registered brands. Painting domestic processing products shall be done before removal from sale area.

All hammer brands and/or yellow paint must remain on logs until they are domestically processed. B-MS may remanufacture such products into different log lengths subject to agreement with Forest Service on surveillance by Forest Service. Remanufactured products to be removed from the area of remanufacture to another facility must be rebranded with the assigned sale brand unless otherwise agreed to in writing by Forest Service. For such remanufactured products, Forest Service may approve use of a State registered brand to be used exclusively as a catch brand, in lieu of the assigned sale brand. B-MS shall pay all surveillance costs except, that Forest Service may waive such payment if such costs are minor and part of normal surveillance activities.

FIRE PROTECTION AND SUPPRESSION

15. Fire Period and Closed Season - Specific fire prevention measures are listed below and shall be effective for the period May 10 to October 20 of each year. The Forest Service may change the dates of said period by advance written notice if justified by unusual weather or other conditions. Required tools and equipment shall be kept currently in serviceable condition and immediately available for initial attack on fires.

16. Fire Responsibility - Bristol-Myers Squibb, or their Agents, hereinafter referred to as the "B-MS," shall: (1) take immediate and independent action to suppress forest fires on the permit area and shall require all working under their permit to do likewise; (2) maintain effective muffler systems or approved spark arrestors on exhausts of all internal combustion engines used in B-MS's operations, unless agreed otherwise.

When requested by the Forest Service, B-MS shall: (1) furnish and maintain in quantities and at locations to be determined by the Forest Service, tool boxes and fire tools to be used used only for suppressing forest fires; (2) Place those working under the permit and the fire equipment at the disposal of the Forest Service for the purpose of of fighting fires at the current Forest Service compensation rates for such services. B-MS shall bear the cost of suppression of fires on the permit area caused by their operations. For Fire caused or permitted to spread due to negligence or fault in B-MS's operations, included but not limited to smoking, warming fires, or failure to comply with fire precautions and requirements of their permit; B-MS shall be responsible for the total cost of suppression and damages.

17. - Normal Precautions. Specific fire precautionary measures are set forth below. Upon request of Forest Service, B-MS shall permit and assist in periodic testing and inspection of required fire equipment. B-MS shall promptly remedy deficiencies found through such inspecting and testing.

The following requirements shall apply during the period May 10 through October 20, inclusive and during other such periods as specified by Forest Service.

1. Fire Extinguishers and Tools Required with Mobile or Stationary Equipment. Each unit of powered equipment, used in connection with this sale, shall be equipped with serviceable tools and fire extinguishers acceptable to Forest Service as follows:

a. Yarders and Loaders

One - Fire extinguisher, dry chemical type of not less than 2-1/2 pound capacity with 4 B.C. or higher rating.

One - 5-gallon standard galvanized metal or fiber glass backpack water container, with hand pump attached, to be filled at all times.

Weatherproofed tool box marked "FIRE ONLY," equipped with a hasp, and containing:

One - Axe, double bit 3-1/2#

Two - Shovels (round point #0 lady or equal) Two - Pulaskis

The tool box shall be mounted on the equipment if possible, otherwise it shall be within 100 feet of the machine at all times when in operation.

b. Dozers, Tractors, and Rubber-Tired Skidders

One - Fire extinguisher, dry chemical type of not less than 2-1/2 pound capacity with a 4 B.C. or higher rating. One - Shovel (round point #0 lady or equal) One - Axe, double bit 3-1/2#, or one pulaski.

c. Trucks, Busses, Pickups, Panels, Automobiles, Service Trucks, or Similar Equipment Used in Transporting Logs, People, Equipment, and/or Materials

One - Fire extinguisher, dry chemical type of not less than 2-1/2 pound capacity with 4 B.C. or higher rating One - Shovel (round point #0 lady or equal) One - Axe, 2# or over, 26-inch minimum length, or one pulaski. One - Bucket or similar water container (at least 1-gallon capacity)

d. Power Saws

One - Shovel (round point #0 lady or equal). Shovel shall be no more distant than the length of the tree on which the sawyer is working.

One - Fire extinguisher, containing not less than 8 ounces of extinguisher fluid or a dry chemical powder type of not less than one pound capacity. The extinguisher shall be carried by

the operator or attached to the saw so as to be immediately available at all times.

Any fueling or refueling of a power saw shall only be done in an area which is free of or which has first been cleared of all material capable of carrying fire; such power saw shall be moved at least 10 feet from place of fueling before starting.

2. Fire Tools on Permit Area. B-MS shall furnish and maintain in serviceable condition, in quantities and at locations to be designated by Forest Service, tool boxes, fire tools, and other fire equipment to be used only for suppressing forest fires. Each tool box shall be weatherproofed and marked "TOOLS FOR FIRE ONLY" and kept sealed. These requirements are in addition to fire tool requirements for mobile and/or stationary equipment.

a. Fire tool boxes shall contain a shovel (round point #0 lady or equal) and pulaski (minimum 3 1/2 # head) for each person engaged by B-MS on the permit area in addition to those tools required for mobile and stationary equipment.

3. Spark Arresters. Each internal combustion engine shall be provided with a spark arrester or spark arresting device approved by Forest Service. Exceptions where Forest Service may approve mufflers or other equipment in lieu of spark arresters qualified and rated under Forest Service standard 5100-1a are: (1) small multi-position engines, such as chain saws, shall meet Society of Automotive Engineers J335b standards; (2) passenger-carrying vehicles and light trucks may have baffle-type muffler with tail pipe; (3) heavy-duty trucks may have a vertical stack exhaust system with muffler, provided the exhaust stack extends above the cab of the vehicle; (4) an exhaust driven turbocharger is considered to be a satisfactory spark arrester. Internal combustion engine exhaust systems, arresters and other devices shall be properly installed and maintained.

4. Blasting. Fuse or prima cord shall not be used unless authorized in writing by Forest Service, with special precautions stated.

5. Smoking. Smoking shall not be permitted within harvest operations except on surfaced or dirt roads, at landings, within closed vehicles, in camps or at other posted places. Smoking shall not be permitted while working or traveling on foot, within or through Sale Area.

6. Precautions for Stoves. Stovepipes on all temporary buildings, trailers, and tents using wood-burning stoves, shall be equipped with roof jacks and serviceable spark arresters of mesh with openings no larger than 5/8 inches. All stovepipes, inside and out, shall not be closer than 2 feet from any wood or other flammable material or 1 foot if the combustible material is protected by a metal or asbestos shield.

7. Debris Around Buildings. The grounds around buildings, tents, and other structures shall be kept free of flammable material for a distance of at least 15 feet from the wall of such structures.

8. Storage of Petroleum and Other Highly Inflammable Products. Gasoline, oil, grease, or other highly flammable material shall be stored either in a

separate building, or at a site where all combustible debris and vegetation is cleared away within a radius of 25 feet. Fire extinguishers and/or sand barrels may be required at such locations specified by Forest Service, when unusually hazardous conditions exist.

9. Debris Burning and Warming Fires. Burning permits shall be required throughout the year for all debris burning fires. Lunch and warming fires may be allowed in fireproofed areas during periods of low fire danger as specified in the fire plan. Such fires shall not be left unattended.

10. Cable Logging. All tail blocks and corner blocks shall be of an accepted haulback design which prevents line fouling and used with line guards. Such blocks shall be located to prevent cables from rubbing against trees, snags, down logs, or rock when operating.

Areas adjacent to blocks shall be cleared of flammable material within a 5-foot radius. One shovel and one pulaski shall be maintained within 10 feet of each block.

11. Emergency Measures. Additional measures and/or other special requirements necessary during periods of critical fire-weather conditions, shall be included in the fire prevention and presuppression plan.

12. Welding. Welding or use of cutting torches will be permitted only in areas that have been cleared, or are free of all material capable of carrying fire. Flammable debris and vegetation must be removed from within a minimum ten-foot radius of all welding and cutting operations. A shovel and a five-gallon standard backpack water container, filled and with hand pump attached, shall be immediately available for use in the event of a fire start.

18. Substitute Measures - The Authorized Officer may by written notice authorize substitute measures or equipment or may waive specific requirements during periods of low fire danger.

19. Compliance with State Forest Laws - Listing of specific fire precautionary measures herein is not intended to relieve B-MS in any way from compliance with the State Fire Laws covering fire prevention and suppression equipment, applicable to operations under this contract, permit or license.

United States Department of Agriculture | Forest Service | R-1

Reply To: 2460 | Date: July 3, 1991

Subject: Interim Pacific Yew Policy

To: Forest Supervisors

Enclosed is an interim policy governing the harvest of Pacific yew and background information on circumstances leading to the proposed policy.

There is presently a growing demand for Pacific yew on those Forests where yew develops into tree form. The bark of Pacific yew is the only approved source of taxol, a chemical that is a promising cancer treatment. Taxol is being developed pursuant to a cooperative research and development agreement between Bristol-Myers Squibb (B-MS) and the National Cancer Institute (NCI).

Because of the limited availability of Pacific yew the Department of Agriculture and B-MS are entering into a cooperative agreement governing the permitting of Pacific yew to B-MS's designated representative from National Forest lands while ensuring the long-term viabilty of the species is maintained.

Some of the key points of the interim policy that you need to be aware of are:

1) Pacific yew will be made avialable non-competively to B-MS through their designated representative, Hauser Northwest, Inc. (Hauser).

2) The instrument used to transfer the yew will be an administrative use permit and there will be no charge for the yew.

3) B-MS in return will reimburse the Forest Service for research, inventory, analysis, and administration costs associated with the yew harvest program as agreed to in an Annual Program Plan which defines the anticipated program and associated costs. Region 6 has the lead on the plan development.

4) The interim policy is based on the cooperative agreement between BM-S and the Department of Agriculture.

/s/ Christopher Risbrudt (for)

JOHN W. MUMMA
Regional Forester

Enclosure
M.Davis:md:lh:6/11/91I CONCUR:M.DAVIS: 6/12/91I CONCUR:M.DAVIS for D.Foth: 6/25/91CONCURRENCE:D.SPORES: 06/25/91

Background

Pacific yew (Taxus Brevifola) has gone from very light demand for specialty products to critical demand as the source for taxol, a drug which shows exceptional promise in the treatment of various forms of cancer. The bark of Pacific yew is the only feasible source for taxol for the next 2-3 years.

Taxol is a complex chemical which inhibits the cell division of certain forms of cancer. Clinical tests with taxol have been very encouraging, demonstrating significant success against recurrent ovarian cancer with a 30-40 percent success rate in patients who did not respond to other forms of treatment and were considered terminal. Because of this high response rate, there is great interest in investigating taxol, in combination with other drugs, in the treatment of ovarian cancer and other major cancers, such as breast and lung, where taxol has also shown positive responses. A number of such studies are in progress but are currently being hindered by an inability to obtain an adequate supply of taxol to conduct the tests. It takes 20,000 pounds of dry yew bark to make one kilogram of taxol. Two grams of taxol are required to treat one cancer patient. It takes 40 pounds of dry yew bark to produce 2 grams of taxol.

Drug supply represents a major problem at this time. Taxol represents the most significant chemical treatment advancement in over a decade. But research and clinical tests necessary for certification by the Food and Drug Administration are being delayed because B-MS, who has been designated by the NCI to commercially develop taxol, has not been able to secure adequate supplies of bark to proceed on schedule.

NCI and B-MS are cooperating in the development of taxol as a cancer treatment under the terms of a Cooperative Research and Development Agreement (CRDA). CRDA's are used when a government agency utilizes the resources, facilities, and expertise of a private company in the commercial development of important new products which have arisen from federally funded research. B-MS had to compete to secure the position of being the sole industrial partner of NCI in the commercial development of taxol.

B-MS has secured the services of Hauser to harvest and collect yew bark for refinement into taxol by Hauser Chemical. Hauser Chemical has chosen by B-MS as they had the most efficient process for converting yew bark into medicinal grade taxol.

The Department of Agriculture is entering into a cooperative agreement with B-MS because the supply of Pacific yew is limited and what is available is critically needed to continue research and development for cancer treatment.

This cooperative agreement serves two principal purposes. First, it is part of a comprehensive federal strategy to ensure that adequate quantities of Pacific yew are available from the National Forests and other public lands to support expeditious research and development of taxol. • Second, it reflects a commitment to maintain the long-term viability of Pacific yew in forest ecosystems throughout its current range.

There are foreign companies in the market for yew for taxol production. The National Forest Management Act (NFMA) provides for the disposal of forest trees, portions of trees or other forest products for research through administrative use when it is in the national interest to do so.

Because it is in the national interest to do so, any permit for Pacific yew harvesting will be first offered to Hauser as B-MS's designated collector. The mechanism for doing so will be administrative use through the cooperative research agreement. As a condition of the cooperative agreement, B-MS has agreed to assist the Forest Service in funding the necessary research, inventory, and analysis needed to ensure that long-term viability of the species is not adversely affected by the harvest of yew needed for taxol production. They have also agreed to assist with funding for the administration of the program.

For the obvious humanitarian reasons, it is essential that we do all we can to make yew bark available while ensuring that long-term viability of the species is maintained. B-MS and NCI need 750,000 pounds of yew bark this year, and an estimated 1,000,000 pounds of bark in 1992.

Taxol is also found in the needles, but in much lower concentrations than in the bark. Test results for the amount of taxol in needles are being rerun because it is felt that taxol in the needles may break down between harvest and testing due to the metabolic action that continues to occur. At this point in time, needles are not an approved source of taxol by the Food and Drug Administration for use on humans in cancer research.

There is, however, another chemical compound present in the needles in much higher concentrations, whose chemical structure is similar to taxol, that scientists are trying to synthetically alter to produce taxol. Other sources of taxol, such as tissue cultures, are also being explored, but leading researchers feel that it will be several years before any breakthrough is made that will produce significant quantities of taxol to reduce the reliance on the bark of Pacific yew.

interim Policy

The interim policy for the harvest of Pacific Yew is based on the cooperative agreement between Bristol Myers-Squibb and the Department of Agriculture. This interim policy is being formulated to ensure that what Pacific yew can be made avialable is offered to B-MS's designated representative, Hauser. The taxol produced from this agreement is to be used for clinical tests leading to the certification of this drug as a cancer treatment approved by the Food and Drug Administration for use on various types of cancer.

Under terms of the Cooperative Agreement and the Annual Program Plan, called for in the agreement, the following interim Policy is to be followed:

1) Pacific yew will only be offered to representatives designated by Hauser with the following exception:

A deminimus (minimum) limit of 10,000 pounds of bark per year can be offered to other companies or institutions for research purposes. This deminimus limit applies to all harvest from National Forest lands and must be approved through the Regional Yew Coordinator to ensure that the national limit has not been exceeded, that the yew is being used to benefit the cancer research effort and is not being exported or held for speculative purposes. There is no deminimus limit associated with needles, tops, and branches which are surplus from Hauser's harvest operations.

2) The means for transfer of Pacific yew will be administrative use under 36 CFR 223.2. An administrative use permit with standard provisions has been developed for this purpose. There is no charge to Hauser for the Pacific yew and the entire tree can be transferred under this agreement. Removal of the wood is optional, but should be encouraged where there is reasonable access and a viable market.

In certain cases you may wish to employ a selective stripping process where only a stipulated percent of bark can be removed, allowing the tree to remain as a living component of the stand.

3) The priority for survey/inventory, analysis, and harvest of yew where yew of 3 inches or greater exists, or is thought to exist, should be as follows:

a) <u>Yew in existing Timber Sale Harvest Units</u>. As a first priority, concentrate efforts in existing harvest units.

<u>Logged Units</u>. The first priority should be units scheduled for burning. Determine, in cooperation with Hauser, the condition of the bark for the extraction of taxol (bark is not moldy, etc.). In those units where bark is of adequate quality and quantity for collection, expedite the removal of the bark prior to burning.

<u>Yew bark within sold harvest units that are not yet logged</u>. The first priority is preharvest of yew bark before the sawlog harvest, if time frames permit.

b) <u>Yew within harvest units on proposed sales on which there is a decision</u>. As a second priority, concentrate efforts within proposed harvest units. Harvest of yew should take place before selling the sale, if time frames permit.

c) <u>Yew outside of harvest units but within the analysis area on proposed and existing sales where there is a decision.</u> As a third priority, assess NEPA documentation as to the compatibility of yew bark harvest. Permit yew bark harvest where documentation adequately covers such areas. Consider supplemental documentation for those analysis areas where additional documentation is deemed necessary.

Concentrate efforts on existing sale analysis areas first and proposed sale analysis areas second.

d) <u>Yew bark from areas where the NEPA decision is under appeal</u>. As a fourth priority, consider harvesting Pacific yew bark from sales where the decision has been appealed but it appears that the harvest of yew bark would not be challenged. Where deemed appropriate, issue a decision to harvest yew bark. Caution - Do not condition the harvest of yew on compromise of the existing sale under appeal.

e) <u>Yew bark from areas currently being planned for future timber harvest that do not have NEPA decisions,</u> As a fifth priority, consider harvesting Pacific yew in areas of planned harvest on which the Decision has not been made. In many cases, these areas will have considerable analysis completed that may help with the decision on the harvest of yew.

f) <u>Yew Bark from areas where there is no analysis planned for other projects, but where the harvest of yew bark would be compatible with the management area direction of the Forest Plan</u>. As a sixth priority, consider harvest of yew in the area described above. Conduct the analysis necessary to insure long-term viability of yew in the ecosystems in which it is proposed for harvest.

g) <u>Yew bark from areas where there is no analysis planned for other projects and the harvest of yew bark would require a non-significant change to the Management Area direction of the Forest Plan.</u> This is the seventh and last priority identified for the potential harvest of yew bark. However, these areas should not be overlooked when planning for areas on which yew can be harvested. Remember that each additional 40 pounds of yew bark harvested may save the life of a person who presently is not responding to other forms of treatment.

Each fall those Forests with harvestable-size yew will be asked to estimate the amount of area that might be available for harvest the following season, and the financing needed for inventory, analysis, and administration to make these areas available. This field season is the best time to plan and scout for next season's opportunities. This information is needed for the Annual Program Plan that is jointly agreed to by the Forest Service and B-MS. The Annual Program Plan is the basis for financing next season's program of operation. It is going to take careful planning to provide the needed yew bark while maintaining the long-term viability of the species in the ecosystems in which it occurs. There are many lives dependent upon the effort that is made. It will be necessary to look toward sources other than existing and proposed sales and plan

for the inventory and analysis necessary. Line needs to give this program high priority.

Project Planning for timber sale and other activities. When scoping new projects with yew of harvestable size, be sure to consider the inclusion of Pacific yew as an issue. Be certain to gather Pacific yew information as part of the normal stand examination process and during cruising so that site-specific data is available on the location and population of yew prior to timber harvest or other activities.

Permits. The vehicle used to transfer Pacific yew to B-MS designated representative Hauser is an Administrative Use Permit in accordance with 36 CFR 223.2. A copy of the permit, along with standard, is enclosed as Exhibit 1. Utilization of the wood is optional but should be emphasized where there is a market for the wood and there is adequate access. The priority is to make bark available for the cancer research effort.

Use pounds dry weight as the unit of measure for bark. For the wood, use cubic feet; conversion factors are being developed for common products such as posts. Do not issue permits for poorly identified or defined areas.

Current Timber Sale Contracts. On existing timber sale contracts, yew has not been listed as an included species under Table A-2. Encourage cooperation between the Timber Sale Purchaser and Hauser collectors with the first objective to be the prelogging of units for yew bark. Yew bark and/or wood can be removed by use of **B 3.41 Material Not in A-2** and **B 8.5 Sale of Other Materials**. In the letter of authorization for removal in using **B** 3.41, state "for disposal to or collection by authorized representatives of Hauser." Do not authorize removal of bark to anyone not authorized by Hauser except in the case where Hauser has been given the opportunity to remove or obtain the bark and has elected not to take the bark.

Future Timber Sale Contracts. It is important that there be no confusion on our intent for Pacific yew on all future timber sale contracts. In timber sale contracts for the regular timber program, Pacific yew should be excluded as an Included Species in A2, 2400-6 & 6T. The disposal of Pacific yew is at the option of the Forest Service through the use of an administrative use permit. Contract Provision B8.5 Sale of Other Materials provides a process for permitting yew, and includes a restriction for not materially interfering with the current contract. Be sure to include information in the prospectus when there is yew of harvestable size that will not be prelogged prior to a sale.

On both current and future contracts, waive cutting yew as part of the whip felling requirement of contract provision C6.4 Conduct of Logging. When permitting the removal of yew, do not condone "high grading" (going a few hundred feet on the uphill side of a road). If high grading occurs, notify the Hauser representative that no permits will be issued to that collector in the future unless they can give assurances that the situation will be rectified.

<u>Documenting Accomplishments</u>. Forest should develop a process to document the inventory, permitting, and harvest of Pacific yew. Track, to the extent possible, the utilization of yew bark from sold regular program timber sales.

<u>Funding</u>. Use timber sale funding to prepare and administer the projects until the transfer of funds from B-MS is accomplished. Code expenditures so that reimbursement of timber funds used for yew projects can be accurately documented. The Forest Service and B-MS are currently negotiating to provide supplemental funding for Forest Service Pacific yew activities.

Use salvage sale funds for yew trees that meet the criteria for salvage funding (FSM 2435).

<u>Regeneration</u>. Pacific yew reproduces successfully by stump sprouting. Promote vegetative regeneration by cutting stumps <u>with bark attached</u> 6-14 inches high.

Consider planting yew as part of the reforestation effort in plant associations where yew is a common component and is not expected to be retained through the planned timber harvest and site preparation processes (Coeur d'Alene Nursery will grow some rooted cuttings this year to gain experience with nursery practices for this species). Collect information on yew stocking during normal stocking surveys to begin building data sets on the survival success of artificial or natural regeneration (sprouts or advance regeneration), use by animals, etc.

<u>Other activities</u>. On precommercial thinning and other timber stand improvement contracts, include specifications that will leave yew.

Consider retention of yew as a very important factor in the final decision on site preparation or fuel reduction treatment (including underburning). Use of fire, chemical, or mechanical treatment may be modified to retain yew in the vegetative structure.

We do not want to promote actions which would adversely impact the long-term viability of the species. The above guidelines will be used for this year's collection efforts in helping meet the demand for taxol.

Through the agreed-upon Annual Pacific Yew Program Plan, inventory of yew on Forest lands will be initiated. In addition, work has begun on the development of a Pacific yew conservation plan which will provide yew bark harvest guidelines for the next few years and still ensure the long-term well being of this species. This work will consider the short and mid-term needs for Pacific yew bark as a source of taxol.

I CONCUR:M.DAVIS:4/12/91I CONCUR:D.FOTH:04/22/91M.Davis:md:lh:6/4/91M.Davis:md:lh:6/11/91I CONCUR:M.DAVIS: 6/25/91

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ECCO______________________ NATIONAL FOREST
ECCO______________________ RANGER DISTRICT

ECCCADMINISTRATIVE USE PERMIT - YEW HARVEST
EC6Ref: 36 CFR 223.2(C), FSM 2463.02

Permit No___

Permission is hereby granted

Hauser Northwest, Inc.
Acting as an Agent for
Bristol Myers-Squibb
78120 Highway 99 South
Cottage Grove, OR 97424

Represented by ______________, Agent & ______________, Collector
______________ ______________
______________ ______________
Ph: __________ Ph: __________

Subject to all the terms and conditions of the Cooperative Research and Development Agreement between Bristol-Meyers Squibb and USDA Forest Service and all subsequent amendments and the annual Pacific Yew Program Plan, and to the conditions listed herein and attached hereto, to harvest and remove bark and other parts from Pacific yew (Taxis brevifolia) from the National Forest lands described below.

1. Termination of this permit will be on ______________________________.

2. Harvest will occur only within designated boundaries.

3. Harvest will not occur within ___ feet of any stream .

4. All Pacific yew trees within the permited area that (are equal to or larger than 3 inches diameter measured at 1 foot above ground) (are marked in the following manner ______________________) are designated for harvest (please xxxxx one out).

5. At a minimum, utilize all bark from cut tree limbs and tops that are 2 inches diameter and larger.

6. Leave stump heights of at least 8 inches but not greater than 14 inches, with bark intact, on all trees cut to promote sprouting.

7. Dispose of harvest residues as directed by a Forest Officer.

8. Supply issuing officer a listing of all authorized peelers and all vehicles associated with harvest operations. Include license numbers and vehicles designated to remove material from Forest.

9. Camping will occur only at locations approved by a Forest Officer.

10. Comply with all other regulations governihg National Forests, including provisions 11 through 16 attached.

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11.EEFire Responsibility - BM-S shall:EE(1) take immediate and independent action to prevent and suppress forest fires on permit area and shall require his employees to do likewise;EE(2) maintain effective muffler systems or approved spark arrestors on exhausts of all internal combustion engines used in BM-S's operations, unless agreed otherwise.

When requested by Forest Service, BM-S shall:EE(1) furnish and maintain in quantities and at locations to be determined by Forest Service, tool boxes, and fire tools to be used only for suppressing forest fires;EE(2) place his men and equipment at the disposal of Forest Service for the purpose of fighting forest fires at the current Forest Service rate of compensation for such services. BM-S shall bear the cost of suppressing fires on permit area caused by permittee's operations. For a fire BM-S caused or permitted to spread due to negligence or fault of operations, shall be BM-S's for the total cost of suppression and damages.

12.EEProtection, Use and Maintenance of Improvements - BM-S, in all phases of harvest operations, shall protect, insofar as practicable, all land survey corners, telephone lines, ditches, fences and other improvements. If such improvements are damaged by BM-S's operations under this permit, BM-S shall restore them immediately to condition existing immediately prior to damage. All roads and trails designated by Forest Service as needed for fire protection or other purposes, shall at all times be kept free of logs, brush, and debris resulting from BM-S's operations. Roads or trails damaged shall promptly be restored by BM-S.

BM-S use of existing roads may be restricted as indicated on Permit Area map.

13.EEConduct of Operations - BM-S shall conduct all operations under this permit in a safe, workmanlike manner, and shall minimize soil erosion and damage to young growth or trees left standing, and take all reasonable precautions to prevent pollution of air, soil, and water.

Permit area map shows areas where specific methods of skidding or yarding are required.

14.EEErosion Control - BM-S shall (1) avoid operating equipment when soil conditions are such that excessive damage will result; EE(2) construct erosion control structures as needed to control erosion; EE(3) repair promptly any existing erosion control structures damaged by BM-S operations; EE(4) complete seasonal erosion control work prior to suspending operations, and EE(5) perform other soil erosion control work as may be required under this permit.

Prior to suspension of operations or seasonal periods of precipitation runoff, BM-S shall remove ruts from roads and construct cross ditches, water bars, water-spreading ditches on landings, roads, and skid trails where staked or otherwise marked on the ground by Forest Service.

Streamcourse Protection - Streamcourses which are subject to this Provision are shown on permit area map unless otherwise agreed, the following measures shall be observed to protect streamcourses.

(a) Operations shall be conducted to prevent debris from entering streamcourse. In event BM-S operation causes debris to enter streamcourses in amount which may adversely affect the natural flow of the stream, water quality or fishery resource, BM-S shall remove such debris as soon as practicable, but not to exceed 48 hours, and in an agreed manner that will cause the least disturbance to streamcourses.

(b) Culverts or bridges shall be required on temporary roads at all points where it is necessary to cross streamcourses. Such facilities shall be of sufficient size and design and installed in a manner to provide unobstructed flow of water and to minimize damage to streamcourses. Trees or products shall not be otherwise hauled or yarded across streamcourses unless fully suspended.

(c) Wheeled or track-laying equipment shall not be operated in streamcourses except at crossings designated by Forest Service or as essential to construction or removal of culverts and bridges.

15.EELandings, Roads, and Skid Trails - Landings, roads and skid trails to be used shall be agreed upon prior to their use;EE and improvements on existing facilities shall not exceed that needed for safe and efficient operations.

Slash, stumps or other debris resulting from improvement of facilities shall be treated or disposed of as slash unless agreed otherwise.

After landings have served BMS's purpose, BM-S shall ditch or slope them to permit water to drain or spread. Unless agreed otherwise, cut and fill banks around landings shall be sloped to remove overhangs and otherwise minimize erosion.

After a temporary road or skid trail has served BM-S's purpose, BM-S shall remove bridges and culverts, eliminate ditches, outslope roadbed, remove ruts and berms, effectively block the road to normal vehicular traffic where feasible under existing terrain conditions and build cross ditches and water bars as staked or otherwise marked on the ground by Forest Service. When bridges and culverts are removed, associated fills shall also be removed to the extent necessary to permit normal maximum flow of water.

16.EEProtection of Historical Sites - Locations of known historic monuments or objects of antiquity protected by American Antiquities Act (16 U.S.C. 433) are shown on permit area map and identified on the ground. BM-S's operations shall be conducted to prevent damages to identified areas.

Discovery of such areas by either party shall promptly be reported to the other party and may by agreement result in permit cancellation.

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I understand and agree that cutting or taking any material under this permit makes all the conditions binding.

Accepted by: ______________________________ Date: ____________
Agent

Accepted by: ______________________________ Date: ____________
Collector

Approved by: ______________________________ Date: ____________
District Ranger

United States Department of Agriculture | Forest Service | R-1

Reply To: 2460/5150 Date: February 27, 1991

Subject: Slash and Site Preparation Treatments in Units with Pacific Yew

To: Forest Supervisors, Nez Perce, Clearwater, Idaho Panhandle, Kootenai, Flathead, and Lolo National Forests

The season for spring burning and site preparation activity is fast approaching. The utilization of yew has emerged as a National issue. I am asking each of you to ensure that burning or site preparation work will not proceed until you have surveyed the units and know that yew bark meeting utilization standards has been removed. If, during the survey, stems or pieces of a utilizable size are found that would be lost during site preparation or burning, the activity will be delayed until salvage of this material has occurred. Notify Hauser Northwest's representative and negotiate a date by which the bark will be removed. If Hauser cannot commit to removing the bark within a reasonable period of time, you should consider removing the stems or pieces by force account and decking the material for later removal by Hauser. Keep track of the costs of this activity as it will be covered as part of the reimbursable bark transfer costs.

Utilizable-size yew is defined as yew 3 inches or greater at the stump. Utilization standards require bark to be stripped to a minimum 1 inch small end diameter at the top of the stem and the branches. An acceptable level of utilization is defined as removal of all bark meeting utilization standards that is reasonably practical to remove. It takes approximately 40 pounds of bark to produce an adequate quantity of taxol to treat one patient. Keep this in mind when determining what is reasonably practical.

I am also asking that you have a prescription for maintaining the amount of yew in the managed stand to follow harvest. This will require protecting stumps, advanced regeneration, and residual trees in stands with utilizable-size yew, or if this not practical or possible, prescribing planting to ensure we maintain yew following harvest. This may require altering site preparation and burning prescriptions to meet this objective. Where possible we should try for natural regeneration. To do this will require pulling slash and debris from around yew stumps and building fire line around residual pockets of yew that are of utilizable size or have the potential to grow to utilizable size. Burning prescriptions need to be cool enough to reasonably protect the yew while meeting your site preparation objectives.

There are a number of activities which are ongoing at this time which you should be aware of: 1) Yew conservation guidelines are being prepared for this coming harvest season. These guidelines will provide the framework for the amount of residual yew that needs to be retained to maintain genetic diversity and biodiversity in those ecosystems in which we may plan to harvest yew. The

guidelines will also call for maintaining yew in the managed stands following timber harvest. The conservation guidelines will be out for review by the end of March and will be out in final form by the end of April; 2) The Regional guidelines are being revised and they will be out by the end of April and will incorporate the direction of the conservation guidelines; 3) The final EIS for the yew harvest program will be out by October of this year. It will address FY 93 and outyear harvest of yew. It will be programmatic in nature and will address the overall issues associated with the harvest of yew. This document is being jointly prepared by Regions One, Five, and Six of the Forest Service with participation by the BLM and the Food and Drug Administration. It will still be necessary to do site specific analysis to address those localized issues and impacts associated with the harvest of yew and then tier to the EIS to address Regional and National issues.

You need to keep focused on the reason we are making yew available and the need to maintain genetic diversity and biodiversity in those ecosystems where we may harvest yew. Our past season's effort was commendable. We do not want to jeopardize public opinion of what we are doing by not salvaging utilizable-size yew that occurs in timber sales, road construction right-of-way or from other management activities. We also need to explore opportunities outside of other management activities where we can make yew available for the National cancer effort.

/s/ JAMES L. HAGEMEIER
for

DAVID F. JOLLY
Regional Forester

I CONCUR:M.DAVIS:02/19/91I CONCUR: C.Walker:02/19/92 I CONCUR FOR D.SPORES: J.NAUMANN:2/24/92

United States Department of Agriculture | **Forest Service** | **RO**

Reply to: 2450/2460 **Date:** October 27, 1992

Subject: Pacific Yew Preharvest Policy

To: Forest Supervisors
ATTN: Timber Sale Contracting Officers

The Pacific Yew Act of 1992 was signed into law on August 7 by President George Bush. This Act mandates management considerations on Federal lands containing Pacific yew to ensure a sufficient supply of taxol while providing for the long-term conservation of the species. The Act requires that:

> ". . . to the extent that timber harvesters' health and safety will not be jeopardized, the bark is harvested from Pacific yew tree in timber sale areas before the harvest of other timber resources.
>
> "Timber . . . harvest activities are carried out in a manner that will minimize any adverse effects on the survival and regeneration of Pacific yew trees."

The Act further requires that:

> "All timber sales awarded after the date of enactment (August 7) and all completed sales before that date, but unharvested on that date are conducted in accordance with the above policy."

Preharvest of Pacific Yew Bark - With regards to the preharvest of Pacific yew bark in Timber Sale Contract harvest units, the following direction applies:

> To the extent that the harvest of yew bark within a Timber Sale Contract harvest unit is consistent with the guidelines contained in "An Interim Guide to the Conservation and Management of Pacific Yew," and when preharvest of the yew bark will not jeopardize the workers health and safety, then Forests will ensure that the Pacific yew bark is harvested prior to other timber.
>
> In those Timber Sale Contract harvest units within drainages where genetic reserves cannot be established as prescribed in "An Interim Guide to the Conservation and Management of Pacific Yew" (Guide Key step 4) due to inadequate density of yew trees, and where yew trees in the sale units have a high probability of being damaged or destroyed during logging of the timber, the yew bark will be preharvested. Otherwise, the yew trees will be protected in compliance with the Interim Guide.
>
> In those Timber Sale Contract harvest units in which a partial harvest is prescribed, 50 percent of the yew stems will normally be reserved as prescribed in "An Interim Guide to the Conservation and Management of Pacific Yew" (Guide Key step 13A). Reserve yew meeting utilization standards which cannot be protected during logging with reasonable effort should be preharvested.

To facilitate the implementation of this direction, Forest Service Contracting Officers will provide timber sale purchasers copies of the enclosed "Notice to National Forest Timber Sale Purchasers."

Prospectuses for new timber sale offerings that meet the requirements for the preharvest of Pacific yew bark should contain information alerting prospective purchasers that the Forest Service will preharvest the yew bark before the harvest of other timber products may begin.

To provide for the orderly removal of Pacific yew bark from timber sales, purchasers should provide the appropriate Contracting Officer/Forest Service Representative with current, specific, information on proposed timber sale harvest dates in accordance with contract provision B(T)6.31 - Operating Schedule, and as applicable, C(T)6.3 - Plan of Operations.

To the extent a timber sale operation is interrupted or delayed for the preharvest of Pacific yew bark, and to the extent the conditions of timber sale contract provision B(T)8.21 - Contract Term Adjustment, are met, an adjustment in time would be granted due to "acts of Government."

When preharvest of Pacific yew is necessary to comply with the Act, the Forest Service will coordinate with Bristol Myers-Squibb's agent, Hauser Northwest, for the removal of the bark prior to the removal of the other timber. It is the Forest Service's and Hauser's desire to have the yew bark removed with little or no disruption in the timber sale purchaser's operation.

<u>Minimize Adverse Effects of Timber Harvest Activities on Yew Trees</u> - Forests will design and administer timber sale contracts so they can be implemented in a manner that will minimize any adverse effects on the survival and regeneration of Pacific yew trees.

Administer existing sales with the intent to meet, to the extent possible, the objectives of minimizing adverse effects on the survival and regeneration of Pacific yew trees.

In planning and implementing future timber sales, be guided by "An Interim Guide to the Conservation and Management of Pacific Yew." Favor logging systems and slash disposal methods that protect residual yew and provide for resprouting of stumps. Where special protection of specific trees or clumps of trees is appropriate, use timber sale contract provisions C(T)2.3 - Reserve Trees, in conjunction with C(T)6.32 - Protection of Residual Trees. Special emphasis will be given to Pacific yew found in green tree reserves and other areas with appropriate designation under the existing timber sale contract.

If you have any questions concerning related operations on existing contracts, please contact Jerry Hofer or Fred Page of this office.

/s/Michael S. Edrington

JOHN E. LOWE
Regional Forester

Enclosure

October 22 1992

NOTIFICATION TO NATIONAL FOREST TIMBER SALE PURCHASERS

The Pacific Yew Act of 1992 was signed into law by President Bush on August 7, 1992. This Act mandates management considerations on Federal lands containing Pacific yew to ensure a sufficient supply of taxol. The Act requires that:

". . . to the extent that timber harvesters' health and safety will not be jeopardized, the bark is harvested from Pacific yew tree in timber sale areas before the harvest of other timber resources.

"Timber . . . harvest activities are carried out in a manner that will minimize any adverse effects on the survival and regeneration of Pacific yew trees."

The Act further requires that:

"All timber sales awarded after the date of enactment (August 7) and all completed sales before that date, but unharvested on that date, are conducted in accordance with the above policy." (The policy referred to is that which would be developed as prescribed by the Act.)

To ensure the preharvest of Pacific yew bark in timber sale contract harvest units, direction of the Pacific Northwest Region is:

Timber harvest units containing yew stems meeting bark harvest utilization standards, currently over 3 inches in diameter, that are not reserved or otherwise designated as leave, will be harvested for bark prior to the commencement of logging activity where this can be accomplished without jeopardy to the health and safety of timber harvesters. The preharvest of the yew bark will be arranged by the Forest Service and conducted by Hauser Northwest, Bristol-Myers Squibb's designated representative. It is the Forest Service's and Hauser's avowed desire to have the bark removed with little or no disruption in the timber sale purchaser's operations.

To provide for the orderly removal of Pacific yew bark from existing timber sales, purchasers should provide the appropriate Contracting Officer/Forest Service Representative with current specific information about proposed timber sale harvest dates in accordance with contract provision C(T)6.31 - Operating Schedule, and as applicable, B(T)6.3 - Plan of Operations.

To the extent a timber sale operation is interrupted and delayed for the preharvest of Pacific yew bark, and to the extent the conditions of timber sale contract provision B(T)8.21 - Contract Term Adjustment apply, a contract term adjustment would be granted. The basis for the adjustment will be "acts of Government."

To minimize adverse effects of timber harvest activities on residual Pacific yew, the direction of the Pacific Northwest Region is:

To administer timber sale contracts so they are implemented in a manner that will minimize adverse effects on the survival and regeneration of Pacific yew trees; and

to give special consideration and emphasis to Pacific yew found in green tree reserves, riparian areas, and other areas defined by appropriate contract language.

United States
Department of
Agriculture

Forest
Service

RO

mike

Reply To: 2470

Date: JUL 1 4 1992

Subject: Policy for the Management of Pacific Yew

To: Forest Supervisors: Klamath, Six Rivers, Shasta-Trinity, Mendocino, Lassen, Plumas, Tahoe, Eldorado and Stanislaus NFs

This letter outlines policy for management of Pacific yew in the Pacific Southwest Region.

Until the Pacific yew Environmental Impact Statement is issued or for the next two years, which ever is first, "An Interim Guide to the Conservation and Management of Pacific yew" will be used to provide guidance in management areas with a genetic reserve where the Pacific yew is being harvested for bark. Recommendations presented in the guide will provide for Pacific yew harvest at levels that will maintain yew populations and available bark supply for taxol production.

On those management areas where Pacific yew occurs, but is not of sufficient size or quantity to allow for bark harvest the Interim Guide does not apply. The goals on these areas are the same as for bark harvest areas: to sustain the Pacific yew gene pool, maintain Pacific yew as part of the diverse ecosystem; and ensure a future source of bark for taxol. During forest operations take precautions to protect the existing Pacific yew.

If Pacific yew trees or stumps needed to maintain yew populations are damaged during regeneration harvest or site preparation operations, evaluate the site to be sure that you are achieving the above stated goals. Where needed, based on this evaluation, plant local yew seed sources or cuttings to maintain yew in the ecosystem. Basically, if Pacific yew is on the site it will be maintained on the site.

When broadcast burning for site preparation for example select leave patches of Pacific yew that can be protected from fire. Pacific yew should be among the species used to reforest the site if it was present at time of harvest.

To implement the Chief's 2430 letter of February 25 (attached) directing the Region to take steps to assure that as much Pacific yew as possible will be available if the extraction of taxol from Pacific yew heartwood becomes feasible the Forests will follow the guidance below:

(The Chief's direction is highlighted, followed by Regional guidance:)

1. **Do not sell Pacific yew wood for any use except research for taxol or minor miscellaneous uses (such as bows, arrows, and minor carving products).**

Follow this direction. There will not be any exceptions.

2. Require removal of Pacific yew wood from all new timber sale contracts after bark removal. The wood must be transported to a secure location.

Bark should be peeled prior to logging. The minimum size piece required to be removed will be 8 feet in length to a small end diameter of 4 inches. The yew wood should be moved to a secure location where it will not be destroyed by site preparation activities and will not be readily available to the general public. The objective is to secure the yew wood for future use.

3. Require that Pacific yew wood be left in the forest or removed to a secure location on all bark collection permits.

Permits issued for peeling bark in timber sale contract harvest units should allow peeled pieces meeting the 8 feet by 4 inch specification to be left in the harvest unit or be moved to secure areas. Any such pieces placed in piles or concentrations should not be in easy access to the public, and should not interfere with future harvest of the other species in the harvest units.

Permits for the yarding of yew logs for later mechanical peeling should provide for removal to a secure area for storing the peeled yew wood meeting the 8 feet by 4 inch specification.

4. Maintain an inventory and location of all wood left in the forest.

Records will be kept on the location, and the estimated amount of yew wood available, for each site where peeled yew wood is known to exist. These records should include the location of peeled yew wood in timber sale contract harvest units, outside of harvest units in general forest areas, and in stock piles. Forests should develop an inventory process that includes the information necessary to later retrieve the peeled yew wood. Forests are encouraged to coordinate the development of their tracking system with neighboring Forests.

Forests should develop procedures to comply with the above until such time as a final decision is made concerning the use of yew heartwood for extraction of taxol.

If you have questions regarding this policy, please direct them to Mike Srago at (415) 705-2697, FTS: 465-2607, DG:M.Srago:R05A.

R J Butler

for RONALD E. STEWART
Regional Forester

Enclosure

United States Department of Agriculture | Forest Service | RO

Reply to: 2460 | Date: January 6, 1992

Subject: Pacific Yew Bark Utilization

To: Forest Supervisors (See Below)*

I consider the effort this Region has made toward the collection of Pacific yew bark during this past year as one of the most successful endeavors we have taken on. Everyone associated with this effort deserves our highest praise. I believe it is important to continue to recognize that the Pacific yew bark program went from almost nothing to three-fourths of a million pounds in the space of a few months. It has been one of those new programs where we have had to learn as we worked through the process. We will continue to learn as we work through the '92 program conservation guidelines and the development of the EIS.

As with any program we undertake, there are critics of National Forest management who continuously look for examples of exception where they can make us look bad through the media. Recently these folks have concentrated on the issue of "waste and mismanagement." The two areas where they seem to be most interested is in the area of utilization of the bark (and needles), and the effect of broadcast burning of stumps and possible retarding the development of new stands of Pacific yew.

We are, with your help, continuing to examine the question of broadcast burning, and will address that more thoroughly in the conservation guidelines. We have depended on Hauser Northwest, in many cases, to determine when utilization was acceptable to some extent. After a review by personnel from this office of some units referenced by our critics, it is apparent that we need to assume more administrative responsibility of the acceptability of utilization. This obviously is even more important when burning of the unit is planned. District personnel should review each unit after Hauser has determined that utilization has been complete, and in those cases where the District feels that additional bark can feasibly be collected, Hauser should be asked to return and finish the collection. There will be situations where there is disagreement, but hopefully these differences can be negotiated. It may also be necessary to have the company finish these units before additional units can be entered. This will shift some of our responsibility and effort to the permit administration process and may increase our total costs, but the effort is necessary.

We are working with Bristol-Myers Squibb on this issue and will work with Hauser Northwest also. Realizing that there is no good way to develop criteria for utilization standards, we will have to develop these with both parties. The emphasis should continue to be to maximize the amount of bark that is feasible to collect.

You will be notified of these meetings with Bristol-Myers Squibb and Hauser Northwest.

/s/ John F. Butruille

JOHN F. BUTRUILLE
Regional Forester

*Olympic, Mt. Baker-Snoqualmie, Gifford Pinchot, Mt. Hood, Willamette, Umpqua, Rogue River, Siskiyou, Siuslaw, and Umatilla NFs

Author:R.Devlin, DG, 12/31/91

United States Department of Agriculture | Forest Service | RO

Reply to: 2460 | Date: November 21, 1990

Subject: Collection of Pacific Yew Bark

To: Forest Supervisors, Colville, Gifford Pinchot, Mt. Hood, Willamette, Umatilla, Umpqua, and Rogue River NF's

The Chief has made an offer to the National Cancer Institute (NCI) to provide it with approximately 60,000 pounds of Pacific yew bark. This offer was made to help meet a short term emergency need for taxol. Taxol is a potential cancer treatment drug currently being tested by NCI. A special effort by the the Forest Service and the Region will be required to accomplish this task.

In order to provide a quick response to NCI's need, an Incident Command (IC) operation is being implemented. I will be designating an Incident Commander in the near future who will be contacting the primary Pacific yew forests very soon to set up the organization and network needed to implement this task.

It will be the function of the IC to identify locations for immediate collection opportunities and to provide the coordination necessary to accomplish the bark collection. Depending on the location and circumstances, collection could be by force account, direct purchase from permittees, short ad service contract, and through the modification of existing timber sale contracts. In all cases, procedures and specifications must be developed and, when necessary, assembled into contract packages.

The primary collection entity for NCI is Hauser Chemical Research, Inc., currently by a contract with NCI. In the future, Hauser will be collecting for NCI's licensee, Bristol Meyers-Squibb. Hauser is currently increasing its bark collection effort. Coordination will be necessary to ensure that there is no duplications or conflicts in our combined efforts.

At this time, we are proposing that collections be confined to units from existing sales, or sales soon to be sold, which have unencumbered NEPA decision documents.

Forests with significant quantities of yew for possible bark harvest are Gifford Pinchot, Mt. Hood, Willamette, Umpqua, and Rogue River National Forests in the Cascades, and the Umatilla and Colville National Forests on the east side. Forests need to designate a lead person who will work with the IC in meeting this commitment to NCI. Send the names of designees to Fred Page, Regional Office, Timber Management.

The compound taxol has been found to be a very promising cancer drug. The use of taxol in clinical test for the treatment of ovarian cancer continue to show positive results. The results from new clinical tests for breast cancer also show promising results. The NCI is presently facing a significant increase in demand for taxol for future clinical tests, a demand that is above and beyond the supply coming from Hauser. The NCI needs this additional supply of Pacific yew bark over the next 2 to 4 months to maintain an accelerated testing process.

This will not be an easy task, but the Forest Service has a reputation for its ability to respond to public emergencies. This effort should be viewed in that context. I urge your support in helping meet this very important and potentially significant contribution to the efforts of the NCI in their continuing fight against cancer.

/s/ John E. Lowe (for)

JOHN F. BUTRUILLE
Regional Forester

cc:Remaining R6 NFsTM WOTM R1
Author:F.Page, DG, 11/16/90

United States Department of Agriculture | Forest Service | RO

Reply to: 2460 Date: October 23, 1990

Subject: Interim Pacific Yew Guidelines

To: Forest Supervisors

Interest in acquiring taxol from Pacific yew for the treatment of cancer patients over the past several years, has generated considerable demand for yew bark from National Forest lands. Although the possibility of growing yew in a controlled environment as a principal source of taxol is being explored, it will be several years before this becomes a reality. In the interim, we must try to be responsive to the needs of the National Cancer Institute for taxol and at the same time assure that Pacific yew, as a forest species, is not exploited and remains a viable component of forest stands.

Interim guidelines for the management of yew are as follows:

1. Permits. Concentrate collections in harvest units or road rights-of-way proposed for a timber sale or those already sold, but not burned. Emphasize utilization of the yew prior to logging to the extent feasible. Do not issue permits for poorly identified or defined areas.

While the sale of yew is a Forest or Ranger District decision and yew may be sold for any product, because of the interest and human values involved in taxol production, we should strive to promote the utilization of the bark along with other portions of the tree bole. Require reasonable utilization of yew that is debarked, so that it is not just "high graded" for only the material that is easiest to get. Bark can be peeled from branches or tops down to approximately 2 inches in diameter.

2. Other activities. Waive cutting yew as part of the whip felling requirement in clearcut units on timber sale contracts. On precommercial thinning contracts include specifications that will leave yew.

Consider retention of yew as a very important factor in the final decision on site preparation or fuel reduction treatment (including underburning). Use of fire, chemical, or mechanical treatment may be modified to retain yew in the vegetative structure.

On new projects be sure to discuss Pacific yew as an issue in the NEPA documentation to ensure that significant issues are captured--where appropriate.

3. Regeneration. In plant associations where yew is a common component and currently is not present in the units, or is not expected to be retained through the planned timber harvest and site preparation processes, consider planting yew as part of the reforestation effort. (Wind River and J. H. Stone

Nurseries will grow some rooted cuttings this year to gain experience with nursery practices for this species.) Collect information on yew stocking during normal stocking surveys to begin to build a data set on the survival success of artificial or natural regeneration (sprouts or advance regeneration), use by animals, etc.

4. Inventory. Be certain to gather Pacific yew information as part of the normal stand examination process, so that site specific data is available on the location and population of yew prior to timber harvest or other activities.

Although Pacific yew is a very widespread minor component of primarily lower elevation stands, we do not want to promote actions which would adversely impact the long-term viability of the species. The above guidelines will provide access to sufficient areas to satisfy the demand for taxol until sources other than wild stand collection can be developed, and still ensure the long-term well-being of this species.

/s/ Tim C. Rogan (for)

JOHN E. LOWE
Deputy Regional Forester

Author:R.Shaffer, DG, 10/1/90I CONCUR:R.SHAFFER:10/02/90I
CONCUR:R.LEASE:10/2/90I concur:S.Burk,10/02/90

United States Department of Agriculture | Forest Service | RO

Reply to: 2460/5150

Date: February 11, 1992

Subject: Pacific Yew Fuel Treatments

To: Forest Supervisors

The burning season is fast approaching, and in some places is already here. In order to ensure that a minimum amount of Pacific yew bark is lost during fuel treatment activities, I am asking that you proceed with burning only after you are ensured that the yew bark has been utilized and the residual yew trees, stumps, and advanced regeneration have been protected.

Forests will survey all proposed burning units and areas to ensure that the yew bark is harvested and the residual yew is protected. Forests are instructed to meet the proposed minimum utilization standards for yew bark harvest, and the current draft conservation guides for the maintenance of Pacific yew in clearcut harvest areas. Following are specific instructions:

Unless otherwise provided for in a yew harvest prescription that designates certain yew to be left, yew bark should be harvested from pieces and stems which have a large end or top-of-stump diameter of at least 3 inches. On such pieces, the bark should be removed to a 1-inch small end diameter at the top of the stem and branches. When yew with harvestable bark meeting these standards is located in burn areas or piles, it should be noted and an estimate of the quantity determined.

Notification of the available yew bark should be made to Houser Northwest. The notification should include the location of the area, the aspect of the area, the estimated quantity, and an estimate of the burning window to assist Houser in scheduling removal.

If Houser does not schedule your request for removal in a timely manner, plan on force account removal with stock piling of pieces. Track force account costs by fund code CWFS, work activity EP, account 50050, and 58 in the last two digits of the other field (xxx xxx 58). Set up your management codes accordingly. Do not burn the pile or area until the yew is recovered.

Further, in areas containing residual yew, broadcast burn only where control can preserve residual yew trees, live yew stumps, and advanced regeneration. Where possible, pull slash away from yew and take other protective measures. Funding of these activities will be consistent with the management purpose for burning.

This effort is required because broadcast burning may kill the residual yew. Special preburning work could include the removal of surrounding fuel, the building of fire lines, or other measures that will keep flames away from the yew trees, stumps, and advanced reproduction. Generally, cool burns in the early spring are more conducive to saving yew than later burns.

/s/ John E. Lowe (for)

JOHN F. BUTRUILLE
Regional Forester

United States Department of Agriculture | Forest Service | RO

Reply to: 2460 Date: February 25, 1992

Subject: Priorities for Spring Yew Harvest

To: Forest Supervisors

This letter provides Regional guidance that will help facilitate the prioritization of areas needing yew harvest early this spring. Enclosed is a "Pacific Yew Harvest Estimates" form, a modification of a form that many of you have already been using. Use this form when requesting yew harvest. This form will provide the consistency in information and data that field units and Hauser Northwest need to prioritize the harvest requests and develop the harvest schedule.

Districts need to identify their immediate needs for yew bark harvest. We have an agreement with Bristol-Myers Squibb and Hauser Northwest to identify our harvest opportunities as follows:

1. Areas where yew harvest is required before burning:

   a. Areas scheduled for burning where yew bark was already harvested, but requires reharvesting to meet yew utilization standards prior to burning.

   b. Areas scheduled for burning which were previously logged for other species.

2. Areas where yew harvest is required before the logging of other species:

   a. Areas scheduled for logging of other species where yew bark was already harvested, but requires reharvesting to meet yew utilization standards prior to logging of other species.

   b. Areas scheduled for logging of other species where yew harvest needs to occur before the logging of other species.

3. Areas requiring reharvest which:

   a. Will not be burned.

   b. Will not be logged for other species in the immediate future.

   c. Are not in timber sale contract harvest areas.

4. Areas where yew harvest will occur outside of timber sale contract harvest areas and the yew bark harvest will be prescribed in accordance with the soon to be published interim conservation biology guides.

Hauser needs information very soon to determine how they will accomplish your high priority yew harvest.

By March 6 provide Hauser with a list of yew harvest areas which will require the most immediate harvest. This list would include areas requiring yew harvest prior to scheduled early spring slash burns or prior to early anticipated logging of other species. Please accompany this list with completed "Pacific Yew Harvest Estimates" for each proposed activity.

By March 30 provide Hauser with a list of your next priority for yew harvest areas. This list would include your next level of urgency for harvesting prior to slash burn or prior to harvest of other species. Also accompany this list with completed "Pacific Yew Harvest Estimates."

/s/ Robert E. Lease (for)

ROBERT J. DEVLIN
Director of Timber Management

Enclosures (2)

cc:
Forest Yew Coordinators
M.Davis, R1
M.Srago, R5
K.Tressider, BLM
David Cox
Mason, Bruce, & Girard
M.Trumbull, Hauser

Author:F.Page, DG, 2/20/92
I concur:S.Burk,02/24/92

United States Department of Agriculture | Forest Service | RO

Reply to: 2460/5150 Date: March 9, 1992

Subject: Pacific Yew Fuel Treatments

To: Forest Supervisors

Some questions have arisen as a result of my February 11 letter regarding Pacific yew and the spring burning program. Of particular concern is the preservation of yew stumps and residual trees or seedlings when prescribed burning is essential for fuel reduction and/or site preparation. The DRAFT Conservation Guidelines, still being developed, have an objective of retaining 50 percent of the yew stumps and other live yew after burning, and an eventual yew stocking similar to the preharvest conditions.

For the protection of live yew stumps and advanced regeneration, the first consideration will be isolation from prescribed burning. It is recognized this will not be feasible in many situations, particularly when you may not be aware of the presence of yew stumps buried in slash. There are numerous examples around the Region where the survival of yew following burning is very successful, so it is possible to design burn prescriptions to favor yew survival.

In units which are burned, a survey will be done to compare survival levels to the preharvest levels. Keep in mind that sometimes the roots or stumps do not sprout for 1-2 years after the burn, so failure to resprout promptly does not always indicate that the stump is dead. Artificial regeneration, through either seedlings or rooted cuttings, can be utilized to provide additional stocking as needed. As with any artificial regeneration effort, the seed (or cutting) source would have to be appropriate for the particular area. Both Wind River and Stone Nurseries are ready to work with Forest personnel on stock production.

With the above clarifications, I believe we can continue to meet the objectives of maintaining yew in the ecosystem while meeting fuel reduction/site preparation objectives. Additional information on utilization standards will be sent out in the near future.

/s/ John E. Lowe (for)

JOHN F. BUTRUILLE
Regional Forester

cc:
A&FM

R.Shaffer:mb:sb;03/05/92
I CONCUR:R.SHAFFER:03/05/92

United States Department of Agriculture | Forest Service | RO

Reply to: 2460 | Date: March 23, 1992

Subject: Pacific Yew Heartwood

To: Forest Supervisors

The Chief's 2430 letter of February 25 directed the Region to take certain steps to assure that as much Pacific yew wood as possible will be available if the extraction of taxol from Pacific yew heartwood becomes feasible. The potential use of the Pacific yew heartwood is based on preliminary findings at the Forest Service's Forest Products Lab where they are exploring methods for obtaining taxol from Pacific yew heartwood. We must be sure that, if a process becomes feasible, Pacific yew wood will not be wasted or used for lower-value products.

The Chief's direction is highlighted below, followed by Regional guidance:

1. Do not sell Pacific yew wood for any use except research for taxol or minor miscellaneous uses (such as bows, arrows, and minor carving products).

There will be times when a demand exists for yew wood products other than "minor miscellaneous uses" that may be met with existing peeled yew in timber sale contract harvest units requiring burning for essential reforestation. To the extent that the timing of the site preparation can be accommodated, and force account removal of the yew wood from these units is not practical (a condition that should be the exception), these yew wood products may be offered for sale. Any such sale should include a required removal date sufficient enough to allow for the essential reforestation, site preparation burning.

2. Require removal of Pacific yew wood from all new timber sale contracts after bark removal. The wood must be transported to a secure location.

Bark should be peeled prior to logging. New timber sale contracts will contain provisions requiring the peeled yew logs to be yarded and decked in a designated area(s). A Regional contract provision requiring the yarding and decking of peeled yew wood is being developed by Timber Management and will be forthcoming soon. The minimum size piece required to be removed will be 8 feet in length to a small end diameter of 4 inches. The yew wood should be moved to a secure location where it will not be destroyed by site preparation activities and will not be readily available to the general public. The objective is to secure the yew wood for future use.

3. Require that Pacific yew wood be left in the forest or removed to a secure location on all bark collection permits.

Permits issued for peeling bark in timber sale contract harvest units should allow peeled pieces meeting the 8 feet by 4 inch specification to be left in the harvest unit or be moved to secure areas. Any such pieces placed in piles or concentrations should not be in easy access to the public, and should not interfere with future harvest of the other species in the harvest units.

Permits for the yarding of yew logs for later mechanical peeling should provide for removal to a secure area for storing the peeled yew wood meeting the 8 feet by 4 inch specification.

4. Maintain an inventory and location of all wood left in the forest.

Records will be kept on the location, and the estimated amount of yew wood available, for each site where peeled yew wood is known to exist. These records should include the location of peeled yew wood in timber sale contract harvest units, outside of harvest units in general forest areas, and in stock piles. Forests should develop an inventory process that includes the information necessary to later retrieve the peeled yew wood. Forests are encouraged to coordinate the development of their tracking system with neighboring Forests.

There are some cutting units where logging is completed and Pacific yew bark has been removed but the Pacific yew wood has not been removed. It is not my intent to prohibit the burning of those types of units where burning is essential for reforestation.

Where practical, peeled yew wood will be salvaged before site preparation or burning. <u>Funding</u> for salvage activities should be provided by the activity requiring the burn. In some cases, such as eminent burning schedules, the unavailabilty of equipment (unit has already been logged and there is not enough yew wood to bring in equipment to salvage wood), lack of benefitting functions funds, and so forth, may not permit us the opportunity to salvage. It is not the intent to prohibit burning these units when the burning is essential for reforestation. Where opportunities exist and time and funding are available, peeled logs meeting the minimum specifications identified above should be moved to a secure location.

Forests should develop procedures to comply with the above until such time as a final decision is made concerning the use of yew heartwood for extraction of taxol.

/s/ John E. Lowe (for)

JOHN F. BUTRUILLE
Regional Forester

United States Department of Agriculture

Forest Service

R-6

Reply to: 2450

Date: April 6, 1992

Subject: Development, C/CT6.405# - Pacific Yew Yarding (4/92)

To: Forest Supervisors

You are hereby authorized to use this new provision, C/CT6.405# - Pacific Yew Yarding (4/92), in all contracts which cover areas in which Pacific yew may be located. We plan to add it to the approved list of provisions at the next update.

With the increasing possiblity of recovering taxol from the heartwood of Pacific yew on a large commercial basis, use of this provision on timber sale contract will help us consolidate and stock pile available material.

We did not want to stockpile unbarked yew because some of the bark is lost through yarding and because of the difficulty of peeling material cut outside the peeling period. The desired sequence of events is to peel yew in units prior to logging and then yard the peeled wood. In doing so, units prescribed to be burned may be burned without destroying yew wood.

Enclosed are copies of the provisions for your use.

/s/ Stephen J. Paulson (for)

JOHN F. BUTRUILLE
Regional Forester

Enclosures

Author:E.Twitchell;hg,4/3/92
I concur:S.Burk,04/03/92I concur:E.Twitchell,04/03/92I concur:J.Hofer,04/03/92

C/CT6.405# PACIFIC YEW YARDING (4/6/92)
In all subdivisions and units shown on Sale Area Map, Pacific yew pieces at least 4 inches in diameter on the small end and at least 8 feet in length, that have had bark removed shall be skidded/yarded, removed and decked at secured locations shown on Sale Area Map or other agreed upon locations.

In the event the Forest Service waives this requirement, Purchaser's Timber Sale Account will be charged at a rate of <$> per acre for acres waived.

R6-2451-C/CT6.405#
4/6/92

INSTRUCTIONS: Approved for use where peeled Pacific yew pieces are present in the cutting unit. Follow Regional guidelines for Pacific yew harvest. The objective is to get previously peeled yew pieces yarded and decked at secured locations from which it may be removed at a later date.

A "secured" location is one that is behind a locked gate, a barricaded road or other similar location. The "secured" location is to be shown on the Sale Area Map.

Appraise estimated cost of Purchaser required work the same as slash work, and convert to a per-acre cost.

When A2 contains "DF and Other Coniferous Species" or something similar, include the wording "Except Pacific yew."

United States Department of Agriculture | Forest Service | RO

Reply to: 2460 Date: June 4, 1992

Subject: 1992 Yew Bark Peeling Season

To: Forest Supervisors, Yew Forests

The Pacific yew/taxol program has been given a high priority for accomplishment as stated by the Chief in his March 9 letter to all employees. Since the season for obtaining yew bark by peeling is a fairly short one at best, there is some urgency associated with making an adequate number of harvest permits available to Hauser Northwest. While it is important to complete rework areas from last year's harvest to bring them in line with current standards, it is also very important to bring new collection areas into the pipeline so that they may be harvested before the prime peeling season is over. Otherwise, we are likely to fall far short of our approved Forest harvest goals for the year, which in turn slows taxol research and has a profound effect on the lives of cancer patients.

In order to expedite the permit process to the extent possible, the following ideas may help:

1. Harvest bark from sold or unawarded timber sales where yew harvest can be done under existing NEPA documentation.

2. Utilize NEPA work previously begun or partially completed for other proposed timber sale areas, including areas outside the actual timber cutting units, where the new guides in "An Interim Guide to the Conservation and Management of Pacific Yew" can be incorporated with a minimum effort.

3. When implementing the guides in an entirely new harvest area, keep in mind that:

a. All the "genetic reserve areas" called for in the Interim Guides do not have to be designated for an entire Ranger District before new harvest can proceed. Only the reserves in those local management areas where the bark harvest would take place need to be designated.

b. While a NEPA decision to harvest bark from an area is subject to appeal for 45 days, harvesting may actually proceed 7 days after the decision document is published.

We recognize that much of the "easy" bark from existing sales was removed last season and that more analysis will be required to harvest on most Forests this year, but we cannot wait for the Yew EIS completion in FY 1993 to help simplify our documentation work. Please stress to your Forest personnel the need to continue to push on this priority program.

/s/ John E. Lowe (for)

JOHN F. BUTRUILLE
Regional Forester

Author:R.Shaffer, DG, 6/2/92
I concur:S.Burk,06/02/92
I concur:F.Page,06/03/92

United States Department of Agriculture **Forest Service** **R-6**

Reply to: 2460 **Date:** April 7, 1992

Subject: Pacific Yew Interim Conservation Guides

To: District Rangers (Thru Forest Supervisors)

For over 6 months a inter-Regional, inter-Agency technical committee has been working to develop guidelines for the management of Pacific yew based on the best research information available and professional judgment to fill in the gaps where data is currently lacking. The product of this effort, a publication entitled "An Interim Guide to the Conservation and Management of Pacific Yew" (March 1992), is being mailed to you under separate cover this week. Due to a somewhat limited supply for the initial printing, non-yew Forests will only receive two copies each for the S.O., while copies will be sent to the Ranger Districts as well on yew Forests.

The guidelines in the publication will be used to direct your management of the Pacific yew program during the upcoming peeling season and until the Environmental Impact Statement for Pacific yew is completed. The DEIS is to be completed this fall. The new "Interim Guides" will replace those provided in my previous letter of March 22, 1991. The new guides address the harvest of needles, as well as bark, should that source for taxol become operational too. The new guides are based upon a "low-risk" management philosophy for yew. By incorporating these new guidelines into your site specific environmental analysis process, we will still be able to provide taxol for cancer patients and maintain yew as a part of the ecosystem.

The guidelines are in the form of a key which should help your staff in application. The rationale in support of the various decisions is also provided to increase understanding. If you have any questions on use or interpretation, please contact Fred Page (326-3538) or Doug Daoust (666-0785).

/s/ Robert J. Devlin (for)

JOHN E. LOWE
Deputy Regional Forester

Author:R.Shaffer,sb,04/06/92
I CONCUR:R.SHAFFER:04/06/91

United States Department of the Interior

TAKE PRIDE IN AMERICA

BUREAU OF LAND MANAGEMENT
Oregon State Office
P.O. Box 2965 (1300 N.E. 44th Avenue)
Portland, Oregon 97208

IN REPLY REFER TO:
5800 (931)

June 4, 1992

Instruction Memorandum No. OR-92-174
Expires 09/30/93

To: DMs, DSDs, and Staff Chiefs

From: State Director

Subject: Fiscal 1992 Pacific Yew Administrative Policies

Attached are new administrative policies authorizing the sale and directing the management of Pacific yew through the remainder of Fiscal 1992. These policies replace Instruction Memorandum No. OR-92-149, issued April 23, 1992.

Please make a revised estimate of the gross pounds of yew bark you expect to produce this season by each category of areas identified for yew harvesting in Section I.B. of the attached policies. This estimate should be submitted to this office (OR 931) on Attachment 2 within two weeks of the date of this memorandum.

To refine our cost estimates, we would like each office to prepare a workload analysis projection for implementing the attached policies for the last quarter of Fiscal 1992. For consistency, the workload analysis must be composed of direct costs only. The analysis should be stated in total months, overtime months, workmonth costs, overtime workmonth costs, and all operational costs (vehicles, travel, per diem, contracts, etc.). The workload analysis must be broken down into three elements:

1. <u>Pacific Yew Extensive Inventory</u>: Include all costs associated with the Pacific yew inventory.
2. <u>Yew Sales and Administration</u>: Include all Pacific yew sale and recovery, yew surveys and tallies, law enforcement, yew propagation, yew budgeting, public affairs, administration, planning, yew meetings, travel and per diem, and any other costs associated with administering the Pacific yew program in accordance with the Fiscal 1991-1992 Annual Pacific Yew Program Plan.
3. <u>Programmatic EIS</u>: Include costs for preparing information for the Pacific yew programmatic EIS.

Specific costs which are to be excluded from your workload analysis are: (1) costs for the removal, handling, and storage of peeled yew logs; and (2) all costs associated with the BLM Pacific Yew Strategy Document.

Forward your workload analysis projection on Attachment 3 to this office (OR 931) within two weeks of the date of this memorandum.

We expect to provide guidance soon for the distribution and cost accounting of the Pacific Yew Account funds we receive from Bristol-Myers Squibb Co. Until then, continue to use special project code PYEW for all Pacific yew program costs except those associated with peeled yew logs and the BLM Pacific Yew Strategy Document in accordance with Information Bulletin No. OR-92-350.

In accordance with the Fiscal 1991-1992 Annual Pacific Yew Program Plan, the only equipment authorized for purchase with Bristol-Myers Squibb contributed funds are (1) scales for weighing yew bark in the field, and (2) computer hardware and software for use by the State Office Biometrician in summarizing Pacific yew inventory data. Any other equipment required in the administration of the Pacific yew program for the remainder of this fiscal year must be acquired with appropriated funds.

Elaine Y. Zielinski

Elaine Zielinski
Acting State Director

3 Attachments
1 - Fiscal 1992 Pacific Yew Administrative Policies (35 pp.)
2 - Pacific Yew Bark Production Estimate (1 p.)
3 - Pacific Yew Program Cost Projection (1 p.)

<u>Distribution</u>
WO (230)(Room 208 LS) - 1
SC (210) - 1
OR (930) - 1
OR (931) - 21
CA (056) - 1
ID (065) - 1
SD, CA - 1
SD, ID - 1

Attachment 1

FISCAL 1992 PACIFIC YEW ADMINISTRATIVE POLICIES

Bureau of Land Management

Oregon State Office

(05/28/92)

FISCAL 1992 PACIFIC YEW ADMINISTRATIVE POLICIES
Bureau of Land Management
Oregon State Office
(5-28-92)

Table of Contents

FISCAL 1992 PACIFIC YEW ADMINISTRATIVE POLICIES
Bureau of Land Management
Oregon State Office

(05-28-92)

Policy Goal: This guidance is established to maximize the recovery of usable Pacific yew from management project areas while maintaining sustainability of the species. Usable yew may be any part of the tree. All reasonable efforts will be taken to prevent waste of Pacific yew resources.

I. TIMBER SALE YEW REVIEW:

To meet the statewide policy goal, it is necessary to establish a systematic timber sale yew review and record keeping procedure. The objectives of a timber sale yew review process are to: (1) maximize the recovery of usable Pacific yew bark and minimize taxol degradation; and (2) prevent the unnecessary burning of potentially usable yew bole wood. Beginning immediately, all existing timber sales and timber sale units felled after December 1, 1990, must go through a review process if a yew tally meeting the standards outlined in these policies does not already exist. All past areas of yew harvest must also go through this review process. Known sites of yew theft are to be included in the review process as well.

A. Procedures: Each district is to develop and implement procedures for surveying usable Pacific yew which are applicable to each project area. These procedures should be specifically designed to achieve the timber sale yew review objectives. See Illustration No. 5 for a Pacific Yew Bark Yield Table.

B. Prioritization: Areas found to contain usable yew following the timber sale yew review are to be classified into one of the following categories listed in order of priority:

1. Yew harvesting required before burning.

2. Approved and unapproved harvest units prior to falling.

3. Theft and yew reharvest areas.

C. Release Certification: If usable yew bark and yew bole wood is not found in timber sale units following the review process using survey procedures established above, a Pacific Yew Survey and Release Certification must be signed by the authorized officer and entered into the timber sale file. Timber sale units having this certification will be "released" for further

management activities. An example of a Pacific Yew Survey and Release Certification may be found in Illustration No. 6.

D. Pacific Yew Database: Accurate and prompt maintenance of a Pacific yew database is critical to the planning and effective monitoring of the Pacific yew harvest program at all levels of BLM management. A standardized automated database has been developed for this purpose. Distribution of software and user instructions will be forwarded under separate cover. For convenience, all Pacific yew hard files should be kept in a centralized location at the resource area or district level.

II. NOTIFICATION OF HAUSER NORTHWEST:

Following prioritization of areas containing usable yew, notify Hauser Northwest in Cottage Grove, Oregon, by certified mail using a BLM Pacific Yew Harvest Notification, Illustration No. 7. The Pacific Yew Unit Survey Report (Illustration No. 8) from the Pacific yew database should be substituted for the BLM Pacific Yew Harvest Estimate Notification once you have the database installed and operating. Be sure to note elevation and aspect on the Pacific Yew Unit Survey Report before mailing to Hauser Northwest. In general, Hauser Northwest will respond within 30 days of receiving a notice of harvestable yew. In cases where immediate action is necessary, Hauser Northwest may be notified by telephone. Those timber sale units having marginal quantities of harvestable yew will be jointly evaluated by BLM and Hauser Northwest to determine the most expeditious means of recovering the usable yew.

III. HARVEST OF PACIFIC YEW:

With the exception of dead Pacific yew trees, there will be no harvest of Pacific yew outside of existing timber sale areas or in any area currently enjoined from timber sales or harvest under District and Ninth Circuit Court order, until further notice. When preparing Pacific yew sales, individual tree and/or unit marking shall be developed to ensure that utilization standards are met.

A. Where Pacific Yew is Reserved to the Government: Sales of Pacific yew which amount to less than $2,500 will be made using a Vegetative or Mineral Material Negotiated Cash Sale Contract (Form 5450-5a or 5450-5). Sales of Pacific yew which exceed $2,499 will be made using a Contract for the Sale of Vegetative Resources (Form 5450-1).

1. Pacific yew harvest contracts will be issued in the following manner: "B-MS, acting through (name of Hauser Northwest or their designated representative), its Designated Agent." A list of designated representatives authorized by

Hauser Northwest for the 1992 peeling season may be found in Illustration No. 9.

2. When using Form 5450-5a and 5450-5, check <u>only</u> box (a) in Section 1. The <u>only</u> exception to this is when yew is sold from BLM storage in accordance with Instruction Memorandum No. OR-92-167.

3. Pacific yew harvest contracts are to be given a six-digit numeric contract number. The first three digits denote the District/Resource Area code as shown in Illustration No. 10. The last three digits are to be serially numbered within each Resource Area, beginning with 001. The following example denotes the first Pacific yew contract number for the Tioga Resource Area: 126-001.

4. In addition to the legal description, list the name of the timber sale from which yew will be harvested.

5. Road maintenance fees will not be required for bark transport.

6. A copy of each Pacific yew harvest contract, including exhibits and supplemental stipulations, will be immediately forwarded to the BLM District Ranger following contract award.

7. Each contract must include the following:

a. An attached map (Exhibit A) clearly showing the area containing yew trees for harvest.

b. An attached Pacific yew tally, including an estimate of total bark yield. The Pacific Yew Unit Survey Report (Illustration No. 8) from the Pacific yew database is recommended.

c. An attached list of standard Pacific yew contract stipulations (see Illustration No. 11).

d. A description of the transport vehicle (make, year, color, and license number) and the name, address, and telephone number of the individual driving the transport vehicle.

B. <u>Where Pacific Yew is Not Reserved to the Government:</u> BLM must rely heavily on timber sale purchasers for accomplishing the recovery of usable bark and yew bole wood. In sold and awarded contracts, it is recognized that BLM cannot legally force purchasers to recover yew resources. However, every effort must be made to remove usable bark from timber sales <u>prior</u> to any timber felling. Removal of yew bole wood will be necessary in circumstances where there is a high probability that it will be

consumed by prescribed fire. Timber sale contract modifications are the recommended means of accomplishing the statewide policy goal. It is understood that the statewide policy goal may be accomplished without contract modifications. However, such modifications will provide the Government with more control over yew harvesting and greater assurance that our policy goal will be achieved. If purchasers are reluctant to have yew bark peeled before timber felling, either by themselves or BLM, contact OSO 931. We have determined that modifications charged against timber sales to harvest Pacific yew do not constitute an augmentation of appropriations.

C. Pacific Yew Harvest Key: The Pacific Yew Harvest Key (Appendix 2) has been designed to guide you through the multitude of existing timber sale conditions for accomplishing the Pacific yew policy goal.

D. Salvage of Dead Pacific Yew: Each office is expected to salvage usable bark from Pacific yew trees killed by thieves or any other cause. The only exceptions to this are yew trees which are still being held as evidence in law enforcement cases and trees which occur in sensitive areas such as Research Natural Areas (RNAs) and Areas of Critical Environmental Concern (ACECs). We have determined that the harvest of dead yew trees qualifies as a categorical exclusion (refer to Illustration No. 12). An environmental assessment and decision record is not needed for salvaging dead Pacific yew trees. However, a written record of the decision to harvest must be made a part of the Pacific yew files. An Optional Plan Conformance/NEPA Compliance Record is suggested for this purpose. This form is found in Chapter III of the H-1790-1 National Environmental Policy Act Handbook as Illustration No. 1.

E. New Timber Sale Contracts: Currently, we are able to proceed with some operations that were previously enjoined (see Instruction Memorandum OR-92-163, Change 3). New timber sales, rights-of-way, and any other authorized operations will be surveyed for Pacific yew. If Pacific yew is present, stipulations shall be included in the contract which reserve the yew to the Government and require peeled yew logs to be moved out of harm's way in circumstances where there is a high probability that they will be consumed by prescribed fire. These stipulations are shown in Illustration No. 13. As with other existing sales, yew bark must be harvested from the above operations prior to any timber felling or other activities which would damage the yew.

F. Sale of Yew to Third Parties: The BLM and B-MS recognize the need to ensure that legitimate research efforts by parties other than B-MS to produce taxol for use in humans be allowed to proceed. The FY 1992 limit for transfer of Pacific yew bark located on BLM lands to parties other than B-MS is 1,000

gross pounds per research project and 5,000 gross pounds of Pacific yew bark overall. If a district receives a request for Pacific yew bark or foliage from other than Hauser Northwest, contact the OR/WA Pacific Yew Coordinator (OSO 931), prior to the sale.

G. <u>Appraised Rates for Pacific Yew:</u> Appraised rates for Pacific yew resources are subject to change. Until further notice, Pacific yew will be sold at the following rates:

1. Wet bark unpeeled, in the woods: $.30/lb.

2. Wet bark when delivered by BLM to Hauser Northwest: $2.24/lb.

3. Yew with bark: $110/ton at the landing; $120/ton delivered to Hauser Northwest.

4. Yew limbs with bark: $.01/gross pound or $20/ton.

H. <u>Sale of Pacific Yew in BLM Storage:</u> Follow the procedures outlined in Instruction Memorandum No. OR-92-167 for selling yew resources from BLM storage. Use a rate of $.01/lb. or $20/ton for yew limbs with bark attached.

I. <u>Sale of Foliage and Debarked Logs:</u>

1. Until further notice, there is no limit on the amount of Pacific yew foliage that may be sold to parties other than B-MS for use in research or development of taxol for use in humans. Debarked Pacific yew logs may be sold to any party, irrespective of their participation in taxol research and development.

2. Appraised rates for yew foliage and debarked logs will be site specific. District cruise/appraisal staff should provide the necessary guidance.

J. <u>Cultural Uses of Pacific Yew:</u> These administrative policies are not to be construed to deny Native Americans of their traditional, cultural use of Pacific yew. It is our policy to continue providing Pacific yew resources to Native Americans for their traditional and cultural uses. If the traditional or cultural use of Pacific yew by Native Americans is non-profit in nature, it may be transferred under free use authority, 43 C.F.R., Subpart 5511.3-7 using Form 5510-1, Free Use Application and Permit.

IV. <u>PACIFIC YEW CONTRACT ADMINISTRATION AND HARVEST ACCOUNTABILITY:</u>

A. <u>Procedures:</u>

1. An Authorized Officer's Representative will visit every area where yew is being harvested from BLM-administered lands to monitor harvest operations and performance under Pacific yew sale contracts. <u>All</u> yew bark, logs, trees, and limbs will be measured and properly tagged with a Pacific Yew Trip Ticket by the Authorized Officer's Representative before it is transported off the contract area by anyone other than an Authorized Officer's Representative. This applies to all Pacific yew, whether reserved to the Government or owned by timber sale purchasers.

2. Spring scales intended for weighing baled hay will be purchased for weighing yew bark in the field. This is the only equipment authorized for purchase by field offices from the Pacific Yew Account.

3. The total measured field weight of each load of bark or the estimated weight of each load of limbs will be entered in the appropriate place on the ticket by an Authorized Officer's Representative and Part E of the ticket placed in the windshield of the transport vehicle. When yew logs or trees are removed by a private hauler, the total number of logs (or trees) will be entered in the appropriate place on the ticket by an Authorized Officer's Representative and Part E of the ticket affixed to a visible location on the load or transport vehicle. The Authorized Officer's Representative will retain Part A of the Pacific Yew Trip Ticket and promptly enter the data into the Pacific yew database upon returning to the office. BLM/USFS Pacific Yew Trip Tickets will be kept in a secured location.

4. While weighing yew bark, the Authorized Officer's Representative will keep a tally of each bag or bundle of bark, noting the serial number of each Hauser Northwest bag tag, the field weight, and the harvester's name (see Illustration No. 14 for a Pacific Yew Bag/Bundle Field Record).

5. Parts B, C, D, and E of the Pacific Yew Trip Ticket will remain with the load until it is weighed on certified scales for payment by Hauser Northwest or their representative. Hauser Northwest or their representative is responsible for promptly returning Part B of the ticket, with the certified weight, to the BLM district office. Parts C and D of the trip ticket are retained by Hauser Northwest and their representatives. Part E of the ticket remains with the load until it is processed by Hauser Northwest.

6. Field weights on Part B of the Pacific Yew Trip Ticket are to be routinely checked by Hauser Northwest or their representative for unusual discrepancies (more than 10 percent) between field weight and certified weight as the load is weighed for payment. District offices must establish a system for reviewing Part B of the tickets to monitor activities of Hauser

Northwest or their representative and to verify that all loads of yew were delivered to Hauser Northwest. The discovery of any unusual discrepancies must be immediately communicated to the BLM District Ranger or, in his absence, the District Yew Coordinator. In addition, appropriate action must be taken in the field until the discrepancy is explained or resolved to the satisfaction of law enforcement staff.

7. In addition to issuing Pacific Yew Trip Tickets, the Authorized Officer's Representative must perform the following duties at each harvest site:

a. Verify that only individuals authorized by the purchaser are doing the peeling.

b. Survey the entire authorized yew harvest site and surrounding areas to be sure that the contractor:

(1) Accomplished full yew utilization under terms of the contract.

(2) Harvested only designated trees.

(3) Adhered to all Pacific yew harvest stipulations.

c. Complete an inspection report which certifies that all known usable yew has been removed from the authorized harvest area and all other terms of the contract have been satisfactorily completed. Refer to Illustration No. 15 for an example of a Pacific Yew Contract Inspection Report. A final inspection report is a prerequisite for completion of the Pacific Yew Survey and Release Certification.

B. Process for Dealing with Noncompliance: The process for dealing with Bristol-Myers Squibb Co. regarding noncompliance is defined in the Annual Pacific Yew Program Plan.

1. If problems or violations of the terms of yew harvest contracts awarded to Hauser Northwest or their designated representatives arise, the Authorized Officer's Representative will immediately notify the responsible parties of the problems or violations and any appropriate corrective action to be taken.

2. If problems or violations persist or are not rectified in a satisfactory manner or time period, the Authorized Officer's Representative may suspend operations under the applicable contract. Thereafter, the District Pacific Yew Coordinator must notify Hauser Northwest of the problem or violation and the response to date.

3. If problems or violations are not satisfactorily resolved after notifying Hauser Northwest, contact the OR/WA Pacific Yew Coordinator (OSO 931).

C. Pacific Yew Contract Modifications, Extensions, and Assignments: Neither the quantity nor price of any Pacific yew sale contract shall be modified. No extension or assignment of Pacific yew sale contracts is permitted.

V. SUPPLEMENTAL PACIFIC YEW INFORMATION:

Effective immediately, each district is to begin collecting information relating to Pacific yew in conjunction with normal stocking surveys and stand exams. Data collected should include seedlings, stump sprouts (one stump with multiple sprouts equals one stump sprout), trees, foliage condition/color, male or female, damage code(s), crown ratio, estimated diameters, numbers of each, and legal description of survey unit. Specific guidance for the collection and maintenance of this information will be forthcoming.

VI. PROTECTION OF PACIFIC YEW:

A. Non-Public Information: We have determined that information relating to specific locations of Pacific yew are classified as non-public (Category 3) under Instruction Memorandum No. 90-457 (Policy for Managing External Access to BLM Records) for purposes of theft abatement. Such information includes inventory maps, Exhibit A maps, Pacific Yew Unit Survey Reports from the Pacific yew database, any TSIS reports identifying Pacific yew in timber sale contracts, and any other information which identifies specific locations of Pacific yew.

B. Theft Prevention Measures: Special measures should be taken to protect Pacific yew trees occurring in areas of high theft risk. Such areas might include parks, ACECs, RNAs, and corridors along mainline roads. This may be accomplished through increased surveillance by BLM personnel during the bark peeling season. Another alternative is to contract with a private crime deterrent agency.

C. Yew Bole Wood: Though contract stipulations are included in these policies for yarding and decking yew bole wood, it is recognized that other less burdensome means of protecting yew bole wood may be available in many cases. You are encouraged to work with timber purchasers in pursuing other less burdensome means of protecting yew bole wood to meet the statewide policy goal. Bole wood should only be removed with yarding equipment in conjunction with normal logging operations. Because research into the extraction of taxol from yew heartwood is incomplete, our yew bole wood policy may change with new research findings.

Appendices:

1. Glossary of Terms
2. Pacific Yew Harvest Key

Illustrations:

1. Sample Letter
2. Stipulation No. 1
3. Stipulation No. 2
4. Stipulation No. 3
5. Pacific Yew Bark Yield Table
6. Pacific Yew Survey and Release Certification
7. BLM Pacific Yew Harvest Notification
8. Pacific Yew Unit Survey Report
9. Hauser Northwest Designated Representatives
10. BLM District/Resource Area Codes
11. Standard Pacific Yew Contract Stipulations
12. Categorical Exclusion
13. Stipulations for Pacific Yew in New Timber Sale Contracts
14. Pacific Yew Bag/Bundle Field Record
15. Pacific Yew Contract Inspection Report

Appendix O

Annotated Bibliography

Appendix O

Annotated Bibliography

A

Alaback, Paul B. 1989. Structure and composition of low-elevation forests in research natural areas of southeast Alaska. Natural Areas Journal. 9(1): 27-39.

Abstract - Pristine examples of low elevation productive old growth forest were studied in permanent plots established in three existing and four proposed research natural areas in coastal Alaska. The study was designed to document changes in the structure and composition of these forests along a latitudinal gradient and to provide a baseline for future studies. To date the research natural areas in coastal Alaska have not been selected to represent the complete range of ecosystem and climatic diversity. Additional research natural areas are needed to represent the diverse geologic and climatic features of this vast region and to provide a more comprehensive baseline to compare against management activities in coastal Alaska and in other forest types.

Allison, Taber D. 1990. Pollen production and plant density affect pollination and seed production in *Taxus canadensis*. Ecology. 71(2): 516-522.

Abstract - Mean pollen production and mean nearest neighbor distance were recorded for several populations of *Taxus canadensis* and correlated with the proportion of ovules pollinated and seed set. Distance and pollen production together explained 86 percent of the variation in pollination success, each variable significantly adding to the regression when adjusting for the other. Seed set was correlated significantly with pollen production and nearest neighbor distance separately, but the multiple regression including the latter two variables was not significant. Seed set was correlated most strongly with pollination success and mean ovule production, suggesting that variation in seed set among *Taxus* populations was a combination of differences in pollen and resource availability.

[Anon]. 1990. [News Brief]. Environmental Defense Fund. September 19. 2 p.

Abstract - This news brief discusses the petition by environmental groups and cancer researchers to list the Pacific yew tree as a threatened species under the Endangered Species Act. The petition was sent to Interior Secretary Manuel Lujan on September 19, 1990. The news brief gives a short history of taxol discovery and its use as a promising new anticancer drug. The brief goes on to state that despite the fact that taxol is in short supply and its source, the Pacific yew tree, is a rare and extremely slow-growing species, neither the Forest Service nor the BLM recognize the tree as "sensitive." Among those groups who signed the petition are the Environmental Defense Fund, the Center for Marine Conservation, Defenders of Wildlife, the National Wildlife Federation, the Natural Resources Defense Council, the Wilderness Society, Friends of the Ancient Forests, and the Oregon Natural Resources Council.

[Anon]. 1990. Pacific yew bark for cancer research. Community Relations Update. Newsletter of Timber Resource Education Inc. December.

Abstract - This article briefly discusses the Pacific yew as the source of the new cancer fighting drug, taxol. The National Cancer Institute is working jointly with Bristol-Myers Squibb to develop this drug. Further, Hauser Chemical Research, Inc. has been selected as the supplier of yew bark and taxol for these efforts. Current taxol collecting techniques and developments are also discussed.

[Anon]. 1991. Government moves to increase taxol supply. Journal of the National Cancer Institute. 83(15): 1054-1056.

Abstract - While taxol has shown great promise as an anticancer agent, the drug is in short supply because of the rarity of its source, the Pacific yew tree. Taxol currently is derived from the bark of the Pacific yew, which is found mainly in the old growth forests of the Pacific Northwest. The article discusses the cooperative research and development agreement signed between the National Cancer Institute and Bristol-Myers Squibb Company. The article also discusses semisynthesis of taxol and future outlook for taxol supply.

[Anon]. 1991. Laboratory scientists mount intensive probe of taxol's mechanism of action. Journal of the National Cancer Institute. 83(13): 904-906.

Abstract - With taxol continuing to show promise as an anticancer drug in clinical trials, scientists are even more determined to completely understand how the compound works. A primary goal is to develop a synthetic substitute for natural taxol. Taxol is a complex molecule. The compound currently is derived from the bark of the Pacific yew tree. Taxol acts as a mitotic spindle poison which interferes with cancer cells' structural apparatus. Most plant-derived anticancer drugs work to stop cell division by inhibiting production of microtubules, but taxol promotes microtubule production and stabilizes them to the point that the cell is unable to divide. Scientists are also trying to define the three-dimensional structure of the molecule. Researchers are using nuclear magnetic resonance imaging and computer modeling in their efforts to understand taxol.

[Anon]. 1991. [News Brief]. Journal of Forestry. October: 8-9.

Abstract - This news brief discusses the awareness of the need for accelerated production of the anticancer drug taxol, while also recognizing concern for the environment. The Bureau of Land Management and the National Forest System both signed agreements with Bristol-Myers Squibb to provide for the collection of bark from the Pacific yew to produce this drug. According to the National Cancer Institute (NCI), sixty pounds of bark—the bark from approximately three yew trees—is needed to produce two grams of pure drug to treat one cancer patient. NCI plans to fund nine to 12 separate projects to produce taxol synthetically and biologically.

[Anon]. 1991. [News Brief]. Journal of Forestry. November: 11.

Abstract - This news brief discusses two avenues of taxol production for fighting cancer. First, a tissue-culture process being perfected by biotechnologists working at Cornell University could produce virtually limitless quantities of taxol in two to five years. Cell lines have been developed that are much more productive than the cells in yew bark in making taxol. Meanwhile, researchers at the USDA Forest Service's Forest Products Laboratory are researching ways to extract taxol more efficiently from the wood as well as the bark of the Pacific yew.

[Anon]. 1991. Pacific yew: the mismanaged miracle. ONRC Journal. Fall: 17.

Abstract - The article states that taxol offers the best hope for an effective treatment for cancer seen in 15 years. However, a problem lies with the Bureau of Land Management and the Forest Service's short-sighted management of the Pacific yew. Full utilization of the yew as one of the management guidelines was not adopted. Small yew trees and bushes have been burned following logging rather than being made available for taxol production. Also, the Forest Service and the BLM have not consistently implemented guidelines giving yew trees the best chance of resprouting after being cut down. Other sources of taxol are currently being developed, including: (1) a process for extracting Baccatin III from needles of the English yew and chemically converting Baccatin into taxol and (2) production of taxotere by Rhone-Poulenc Rorer. About ten times as much taxol can be produced from English yew leaves as from as from Pacific yew bark.

[Anon]. 1991. [News Brief]. Taxol Summary. National Cancer Institute. Rockville, Maryland. February 6. 2 p.

Abstract - This newsbrief gives a history of taxol isolation and production, and discusses current drug supply. Taxol, a plant-derived anticancer drug, was first isolated from the western yew tree, *Taxus brevifolia.* It is also found in other members of the genus. Clinical trials with taxol have been encouraging, with a 30-35 percent response rate in over 200 patients suffering from recurrent ovarian cancer. The National Cancer Institute has signed a cooperative research and development agreement with Bristol-Myers Squibb Company. Large numbers of yew trees are necessary for extracting significant amounts of taxol. For this reason, other methods of extracting and synthesizing taxol are being pursued. Researchers are investigating such approaches as propagating high-yielding yew specimens, cultivating plant tissues, and semi-synthesizing taxol.

[Anon]. 1991. [News Brief]. U.S. Fish and Wildlife Service, Region 1. January 9. 2 p.

Abstract - Citing abundance of trees and few threats to the species, the Fish and Wildlife Service declared there is not enough scientific evidence currently available to list the Pacific yew as a threatened species. The agency claims the Pacific yew exists on at least 2.5 million acres of land in California, Idaho, Oregon, and Washington. Environmental groups requesting the listing claim the yew exists on only 1.2 million acres in the lower 48 states. Despite its commercially viable status as a source of the cancer-fighting drug taxol, and the fact that few laws protect it, the Fish and Wildlife Service says no substantial case has been made to warrant listing at this time. The Fish and Wildlife Service will consider the status of the species, and not the need for the abundance of taxol, in judging whether to propose listing. The agency was petitioned in September, 1990, by the Environmental Defense Fund, the Center for Marine Conservation, and two medical researchers.

[Anon]. 1992. [News Brief]. Weyerhaeuser Company. January 8: 1 p.

Abstract - This news brief discusses the supply agreement recently signed between the Weyerhaeuser and Bristol Myers-Squibb companies. Weyerhaeuser is to become a future major supplier of taxol-containing yew trees over the next 10 years. Weyerhaeuser will grow large numbers of yew trees in its western nurseries. In addition to the supply agreement, Weyerhaeuser signed a cooperative research agreement with Bristol Myers-Squibb in August, 1991, to determine whether cultivating domestic yew trees would be viable for taxol production. The supply agreement and the research agreement are closely linked. Weyerhaeuser's research efforts are partially funded under a competitive grant from the National Cancer Institute. Weyerhaeuser has established the largest Pacific yew genetics nursery study currently in existence.

[Anon]. [n.d.]. Trees and tall shrubs. In: Poisonous garden and crop plants. Chapter IV. 162-163.

Abstract - These two pages discuss the yew, or ground hemlock. Included are: quick identification check tips, description, occurrence, toxicity, treatment, and notes.

Antos, Joseph A.; Habeck, James R. 1981. Successional development in *Abies grandis* (Dougl.) Forbes Forests in the Swan Valley, western Montana. Northwest Science. 55(1): 26-39.

Abstract - *Abies grandis* is abundant and is potentially a climax species over a major part of the Swan Valley in western Montana. This area is among the easternmost extensions of wet, low-elevation forests related the Pacific maritime climatic influence. Species coverage and site parameters were ascertained on 56 natural stands representing a wide range of site conditions and stand ages. The stand data were analyzed using polar ordination techniques. Site moisture status and successional development are the most important factors determining species composition among the *Abies grandis* forests studies. Few, if any, stands have reached climax status due to the repeated occurrence of fire. After intense fires, *Larix occidentalis* and *Pinus contorta* become established. When stands over 150 years old burn, *Larix occidentalis*

tends to predominate in the regeneration; if the stands are young, *Pinus contorta* tends to be favored. *Abies grandis* typically forms a layer below the *Larix occidentalis* or *Pinus contorta* canopy. Tree compositional changes along synthesized developmental pathways and understory alterations are discussed.

Austermann, Kurt. 1992. Seed orchard cultivates Pacific yew. BLM News, Oregon and Washington. United States Department of the Interior, Bureau of Land Management. Oregon State Office. Portland, Or. January. P. 2.

Abstract - Researchers at the Bureau of Land Management's Charles A. Sprague Seed Orchard are attempting to propagate Pacific yew trees through seed stratification. The nursery currently has 300 seeds in storage. The Pacific yew has recently become a valuable resource because its bark has been found to contain taxol, a successful anticancer compound.

Atzet, Thomas; Wheeler, David L. 1984. Preliminary plant associations of the Siskiyou Mountain province. USDA, Forest Service. Pacific Northwest Region.

Abstract - This publication is the first approximation of the plant associations in the Siskiyou Mountains and the result of the Area Five Ecological Program to classify Forest Service administered lands. It is a guide documenting the first of two phases of classification: floristic classification and description. (Phase two, the predictive phase, provides plant response information such as growth, yield, successional pathways, and potential productivity.)

B

Bolsinger, Chuck. 1990. Material for a state-of-knowledge paper on Pacific yew (which is detailed in a paper to be published in the Silvics Manual). PNW—FIA.

Abstract - This information on the Pacific yew is presented in three categories: (1) distribution, abundance, and ecological setting of Pacific yew; (2) inventorying Pacific yew on National Forests—some considerations; and (3) conservation/protection considerations. This paper also addresses an "apparent inconsistency" between Thomas Spies' paper on plant species diversity in old growth and FIA data that show yew to be present in 500,000 acres of young growth stands.

Bolsinger, Charles L.; Jaramillo, Annabelle E. 1990. *Taxus Brevifolia* Nutt. Pacific Yew. In: Silvics of Forest Trees of North America. R.M. Burns and B.H. Honkala, Tech. Coordinators. USDA Forest Service. Agricultural Handbook No. 654. Vol. 1, Conifers. Washington, DC. December: 573-579.

Abstract - Pacific yew, also called western yew, is a coniferous tree associated with several conifer and hardwood tree species on a variety of sites. Pacific yew tolerates shade, and in undisturbed stands is usually found as an understory tree. Growth of such trees is slow, but where the overstory has been removed or thinned, diameter growth on undamaged yew trees may increase considerably. Pacific yew rarely exceeds 60 cm (24 in) in d.b.h., and 15m in height. The largest on record is 142 cm in d.b.h., and 18m in height. The wood is hard, heavy, and resistant to decay. Although not of great interest to the forest products industry, it has many special uses. Because the bark of Pacific yew contains a drug, taxol, that is being used in cancer research, demand for yew bark by the National Cancer Institute has increased dramatically in recent years.

Borman, Stu. 1991. Scientists mobilize to increase supply of anticancer drug taxol. Chemical & Engineering News. September 2: 11-18.

Abstract - This article first discusses a brief history of the discovery and development of taxol as a cancer fighting drug. Problems lie within the fact that the current source of taxol, the Pacific yew, is in limited supply. The author goes on to discuss alternative ways scientists are working to increase the supply of taxol. The French pharmaceutical firm, Rhone-Poulenc Rorer, is currently developing a taxol analog, taxotere. Taxotere begins with a taxol precursor isolated from yew needles. Another strategy being investigated to increase taxol availability is direct extraction of the compound itself from yew needles. Researchers at the Forest Service's Forest Products Laboratory at Madison, WI are studying extraction of taxol from the heartwood of the Pacific yew. Another possibility is obtaining taxol from *Taxus* plants grown for ornamental use instead of the wild. The concept of producing taxol in cultures of cells grown in bioreactors is also being investigated.

Brady, Timothy J. [1985 rev.] Field key to the conifers and taxads of British Columbia, Washington, Oregon, and northern California. Seattle, WA: Department of Botany. 1-7.

Abstract - This guide provides, in outline form, descriptions of both conifers and taxads found in the Northwest. Included are (1) both scientific and common names and (2) descriptions of bark, leaves, and other identifiers. A glossary is also provided.

Bristol-Myers Squibb Company. [n.d.] Taxol Q & A. New York, NY. 10 p.

Abstract - Several questions and answers regarding taxol are provided. These questions and answers are divided into five subheadings; Background/General Information, Research & Development, Cooperative Agreements With The U.S. Government, Environment/Supply, and Alternative Sources. These questions and answers are provided by Bristol-Myers Squibb Company.

Bristol-Myers Squibb Company. [n.d.]. The search for alternative sources of taxol. New York, NY. 4 p.

Abstract - This paper discusses the most promising research leads which are expected to provide some relief from the need to use yew bark for taxol production within two to three years. One alternative, biomass, refers to the renewable parts of the yew, such as leaves and twigs. These parts would be used to extract taxol, though their yield would probably not be sufficient. Semi- and total synthesis is also being researched. In the future, taxol might be produced by extracting a taxol molecule from the leaves of readily available yew plants. Scientists are also working to produce taxol from the cells of fast-growing parts of the yew tree, "plant cell culture." Finally, the feasibility of developing yew plantations is being investigated. A timetable is also provided.

Brody, Jane E. 1990. Gardens of plant tissue in labs seen as factories for vital drugs. The New York Times, Science. November 20.

Abstract - This article describes taxol, derived from the bark of the Pacific yew, as one of the most promising anticancer drugs to be tested in years. Due to the limited natural supply and futile synthesizing efforts, researchers have turned to tissue culture, reproducing in the laboratory bark cells that can produce large amounts of taxol. By manipulating plant cells and growing mediums, researchers can create vast laboratory gardens of plant parts that produce important chemicals quickly, cheaply and reliably in a confined space. The goal is to create a "forest" of bark from the Pacific yew without having to destroy a single tree.

Brown, H.P., et. al., 1949. Textbook of Wood Technology. 1st Ed. New York: McGraw-Hill Book Co., Inc. p.506.

Abstract - Discusses uses of yew wood (poles, bows, canoe paddles, etc.).

Byrnes, Patricia. 1991. Are we killing a cure for cancer? Wilderness. Summer. 54(193): 4.

Abstract - Conservation groups claim that the Forest Service and BLM are not properly managing the Pacific yew as a valuable resource. Until the Pacific yew was found to contain taxol, a promising new anticancer drug, the tree was considered worthless by foresters and timber companies. Yews were discarded as "weed" trees and left to burn on slash piles. Because yews exist mainly in the old growth forests of the Pacific Northwest, as little as 10 percent of the original stands may remain. The Wilderness Society has urged the Forest Service and BLM to create a special task force to deal with the Pacific yew controversy, and to create a viable and environmentally sound means of managing the trees. The Wilderness society is concerned that trees and taxol are being wasted because the federal agencies do not have a clear idea of how to manage the remaining stands of native Pacific yew.

C

Calder, James A.; Taylor, Ron L. 1968. Flora of the Queen Charlotte Islands, Part 1: systematics of the vascular plants. Research Branch, Canada Department of Agriculture. Monograph No. 4 Part 1: 161-162, 558.

Abstract - *Taxus brevifolia*, found on Graham Island and Moresby Island of the Queen Charlotte Islands, is briefly described. A map is also provided, showing where *Taxus brevifolia* can be found.

Campbell, Robert K. 1979. Genecology of Douglas-fir in a watershed in the Oregon Cascades. Ecology. 60: 1036-1050.

Abstract - To gain insight into genetic microstructure of subregional populations of coastal Douglas-fir, genetic variability in a population found on a 6100-ha central Oregon watershed is described. Genotypic values of 193 parent trees located throughout the watershed were estimated from progeny grown in a common garden. Then, genetic cariation was partitioned into components attributable to parent-tree location and to differences among trees within locations. Within-location variation appeared to be homogeneous in the watershed; depending on the trait measured. Although other possibilities exist, the topoclinal variations are due to high selection intensities in the seedling stage, the former to selection by average environmental differences along gradients, the latter to microenvironmental heterogeneity. The combination of high within- and between - habitat variation is suited to a species which episodically colonizes an environment that is extremely heterogeneous in time and space.

Cannon, Bill. 1992. The ugly sapling: wonder drug from trash tree? Columns. March: 20-23.

Abstract - This article describes an outing by University of Washington scientists to take study samples from the world's largest recorded Pacific yew tree, located on the Gifford Pinchot National Forest. The article also discusses yew natural history and some of the current issues surrounding yew trees and the cancer-fighting

drug taxol. Until they were discovered to contain taxol, yew trees were considered to be "trash trees" by forest harvesters. Scientists are unsure as to how many yew trees may be harvested for taxol without destroying the species. Scientists hope to find new ways of extracting and producing taxol in order to minimize the need to use live trees. Heinz Floss, a chemistry professor at the University of Washington, is working under a $26,000 grant from the American Cancer Society to biologically synthesize taxol. The article also includes a brief sidebar by Cheryl Dawes describing the University of Washington's "compassionate use" program, a taxol cancer treatment program for women whose ovarian cancer had not responded to at least three courses of chemotherapy.

Chadwick, L.C.; Keen, R.A. 1976. A study of the genus *Taxus*. Wooster, Ohio: Ohio Agricultural Research and Development Center.

Abstract - The taxonomy of the genus *Taxus* is controversial. The recognized species are more geographic than morphologic and many of the cultivars and clones in America have not been described or named by horticulturists in accord with the International Code of Nomenclature of Cultivated Plants (2). This publication aids in furnishing descriptive information of many of the cultivars now in the trade. It includes sections on propagation and culture.

Chang, Ying-Pe. 1954. Bark structure of North American conifers. USDA, Forest Service. Technical Bulletin No. 1095. 86 p.

This study, which was a 1951-52 project of the U.S. Forest Products Laboratory, dealt with the comparative anatomy of North American coniferous barks. Its general objectives were essentially the following: (1) To determine the basic anatomical structure of all tissues outside the cambium of matured barks; (2) to evaluate the features of bark structure of diagnostic value and other related findings from bark as means for identification of species; and (3) to induce the viewpoints that would correlate bark structure to related research in the field of forest products.

Coley, Phyllis D.; Bryant, John P.; Chapin, F. Stuart-III. 1985. Resource Availability and Plant Antiherbivore Defense. Science. 230(4728): 895-899.

The degree of herbivory and the effectiveness of defenses varies widely among plant species. Resource availability in the environment is proposed as the major determinant of both the amount and type of plant defense. When resources are limited, plants with inherently slow growth are favored over those with fast growth rates; slow rates in turn favor large investments in antiherbivore defenses. Leaf lifetime, also determined by resource availability, affects the relative advantages of defenses with different turnover rates. Relative limitation of different resources also constrains the types of defenses. The proposals are compared with other theories on the evolution of plant defenses.

Congress of the United States Office of Technology Assessment. 1991. Biotechnology in a Global Economy. October: 73-96.

Abstract - This report discusses the development of biotechnology-based pharmaceutical products. The report focuses mainly on the business aspect of biotechnology and the pharmaceutical industry. It is divided into four main sections, which include entries on research and development, biotechnology-derived drugs, and competitive factors. The biotechnology industry is proving to be quite important in the discovery of new drugs. Currently, the commercialization of biotechnology is highly dependent on market forces.

Cordell, G.A. 1992. Novel strategies for the discovery of plant anticancer agents. Program for Collaborative Research in the Pharmaceutical Sciences, Chicago: Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, University of Illinois at Chicago. 60612.

Drug discovery involving plants has been a pursuit of mankind since prehistoric times. Through previous efforts, plants established as being a viable source of clinically useful compounds (e.g. vincristine), have afforded leads for synthetic modification (e.g. camptothecin) and have served as tools for mechanistic studies. In

this presentation, some previous studies will be reviewed and a new strategy for the discovery of anticancer agents from plants will be described in which ethnomedical information is correlated with pertinent published chemical and biological information, resulting in a prioritization of plants for collection. Authenticated plants are extracted and the extracts tested in a broad cooperative research program involving a university, a research institute and a pharmaceutical company. Bioactivity-directed fractionation is carried out at all three sites, with a view to identifying novel compounds which may serve as candidates for preclinical testing.

Cragg, Gordon M.; Boyd, Michael R.; Cardellina, John H. [and others]. 1992. Role of Plants in the National Cancer Institute Drug Discovery and Development Program. Bethesda, MD: Developmental Therapeutics Program, National Cancer Institute (NCI). 20892.

Over the past 30 years, NCI has developed a number of clinically active plant-derived drugs. Prior to 1986, collections were generally restricted to temperate areas of the world. Since then collections have focused on tropical (primarily rainforest) regions and over 27,000 samples have been collected from over 25 countries. Policies have been formulated aimed at establishing collaborations with scientists in these countries, and providing long-term compensation for drugs which are developed as marketable products. The various facets of the drug discovery and development program will be discussed, including future plans for the large-scale production of promising new anticancer and antiviral natural products (e.g. taxol and camptothecin derivatives).

Crawford, Rex Charles. 1983. Pacific yew community ecology in north-central Idaho with implications to forest land management. Forest, Wildlife and Range Experiment Station: University of Idaho. 109 p. Ph.D. dissertation.

Abstract - *Taxus brevifolia* (Pacific yew) develops into dense stands in north-central Idaho, deviating from its usual occurrence as a scattered, small tree or shrub in mesic forests of the Pacific Northwest. Approximately 16,000 hectares of forest land in the South Fork of the Clearwater River basin Idaho are occupied by *T.*

brevifolia communities. Twenty-seven mature, undisturbed *T. brevifolia* stands were surveyed for physiognomy, vascular floristic composition, species cover, tree population structure and physical soil characteristics. These stands were analyzed and compared with 26 adjacent undisturbed, mature *Abies grandis* communities. Analysis of tree population structure indicated that *T. brevifolia* is the climax dominant. It showed more success in self-replacement in the absence of major disturbance than any conifers. The *T. brevifolia* habitat type occurs on warmer sites with shallower soils than the *Abies grandis* habitat type. *T. brevifolia* trees survive logging operations and will adapt to unshaded conditions.

Crawford, Rex C.; Johnson, Frederick D. 1985. Pacific yew dominance in tall forests, a classification dilemma. Canadian Journal of Botany. 63: 592-602.

Abstract - A review and discussion of the confusing terminology for units designating variation in vegetation associations (habitat types) are presented. In portions of the northern Rocky Mountains, the short tree *Taxus brevifolia* is presented, concluding that associations and not phases are the appropriate interpretation. Binomials now used in forest classifications conceal information on community structure and composition. Trinomials are proposed.

Curtis, Cynthia; Bray, Anne, compilers. 1987. Boatbuilding woods: a directory of suppliers. Woodenboat Magazine.

Abstract - Boatbuilding woods available in the U.S. are listed by state and species sold by dealer. Several are listed for Oregon and Washington.

D

Daly, Douglas. 1992. Tree of life. Audubon. March/April: 77-85.

Abstract - This article gives a general history of taxol discovery and supply; some yew natural history is discussed. Taxol, a compound found in the bark of the Pacific yew tree, has proven successful as an anticancer agent. Supply is short and cancer patients are desperate to receive the drug. The author comments on the irony of the situation. Until recently, the yew was thought by foresters to be a worthless "weed tree," and was often left to burn in slash piles after logging. The social, economic, and political impacts of taxol discovery and yew harvest are discussed. Two sidebars are included with the article. One gives a brief discussion on Canadian yew exports to the U.S. The other discusses the toxicity of taxol, and explains that often the difference between a cure and a poison is the dosage. Taxol does have side effects, some serious, which include bone-marrow toxicity, loss of white blood cells, aching muscles, hair loss, diarrhea, nausea, vomiting, and rarely, cardiac and central neuro-toxicity.

Developmental Therapeutics Program, Division of Cancer Treatment National Cancer Institute. 1990. Bethesda, MD: Workshop on taxol and *Taxus*: current and future perspectives. June 26.

Abstract - This volume includes abstracts of all speakers who presented at this workshop on taxol and *Taxus*. There is also a list of participants with their addresses and telephone numbers. The remainder of the book is broken down into six sections: Agronomics, Chemistry, Clinical Studies, Biological Production, Biological Effects, and R&D Support. Each section includes "Taxol Workshop Information Sheets" which allow individuals to address their area of taxol interest, summary of current work and future plants, and areas in which they are seeking collaboration.

E

Eblin, James B. 1991. The Yew and We. A paper prepared in partial fulfillment of the requirements for Professor Stark Ackerman's Forest Law and Policy Seminar, Lewis and Clark Northwestern School of Law. 24 p. Seminar Paper.

Abstract - This paper presents the history and background of various views on the yew/taxol controversy. While presenting and exploring ethical issues, Eblin provides an overview of *Taxus brevifolia* and the drug taxol. Eblin begins with an explanation of yew taxonomy and eventual classification in the family Taxales. He briefly delves into yew cultural background and also covers the evolution of taxol into a breakthrough cancer drug; the petition to list yew as a Threatened and Endangered species; the relationships between the National Cancer Institute, Bristol-Myers Squibb, Hauser, the Forest Service, and the Bureau of Land Management; alternative sources of taxol; the non-use of needles as a source; bark collection; and his prediction of the future and commentary on the present. Eblin forecasts that the Forest Service will allow harvest in HCAs based on a pattern of allowing the maximum productive utilization permitted under the rules.

Environmental Defense Fund. [n.d.]. Fact Sheet on the Pacific Yew (*Taxus brevifolia*). Washington, DC. 2 p.

Abstract - This fact sheet includes 15 short paragraphs with historical, technical, and statistical information about the Pacific yew and taxol. The Pacific yew is found to exist mainly in the old growth forests of the Pacific Northwest. The tree is an understory species, depending on cool, moist habitats. Much of the yew's habitat has been destroyed by clearcut logging operations. Neither the Forest Service nor the BLM currently treat the Pacific yew as a "sensitive" species. The bark of the yew contains an important cancer-fighting compound called taxol, found to be effective in treating ovarian and possibly several other types of cancer. The fact sheet goes on to suggest that the tree be listed as a threatened species under the Endangered Species Act. Federal listing would force the U.S. Fish and Wildlife Service to restrict commerce in the species. Listing the Pacific yew would ensure its survival as a species.

Environmental Defense Fund. [n.d.]. EDF Fact Sheet. Washington, DC. 1 p.

Abstract - This fact sheet on the Environmental Defense Fund is divided into four sections. They include: EDF at a Glance, EDF Goals, EDF Successes, and EDF Offices.

Environmental Defense Fund. 1990. Petition to Secretary Manuel Lujan. Washington, DC. September 19. 12 p.

Abstract - This petition sent to Interior Secretary Manuel Lujan requests the listing of the Pacific yew tree as a threatened species under the Endangered Species Act. The petition is signed by eight environmental groups and three scientists. The document cites four main reasons for listing the yew. They are as follows: I. "Because the Pacific yew occurs principally within ancient forests and those forests have declined substantially over the past century, the yew is today a depleted species." II. "The Pacific yew is extremely vulnerable to logging operations and is being further reduced with liquidation of the ancient forests." III. "It is imperative that the Pacific yew be afforded protection since it currently serves as the major source of the anticancer compound taxol, and it will enhance efforts to produce an alternative source of taxol." IV. "Addition of the Pacific yew to the list of threatened plant species will authorize federal agencies to protect the species from habitat destruction and commercial exploitation." The document is footnoted and referenced.

Environmental Defense Fund. [n.d.]. Some Questions and Answers. Washington, DC. 3 p.

Abstract - This question and answer sheet briefly discusses the Pacific yew as a source of taxol, a promising new anticancer compound. Two questions are addressed. The first relates to the consequences of listing the yew tree as a threatened species under the Endangered Species Act. The second discusses various other plant-derived pharmaceutical compounds and their contributions to society. A partial list of plant-derived medicines currently in use is also included.

Erikson, Deborah. 1991. Secret garden, cell culture may provide a unique route to taxol. Scientific American. October: 121-122.

Abstract - Taxol will not be useful as a widely used cancer drug until it is produced in mass quantities. Using the bark of the slow-growing Pacific yew tree is not a long-term solution. Scientists are attempting to make taxol from cultures of yew cells. The National Cancer Institute recently awarded a $1.27 million grant to develop methods for mass production of taxol through cell culture. Scientists predict that a large scale tissue cell culture system will be working within the next two to three years. If cell culture proves successful, other botanical drugs may be produced in mass quantities.

F

Fackelmann, Kathy A. 1992. The Adjuvant Advantage. Science News. February 22: 124-125.

Abstract - Women with early stages of breast cancer may increase their chances of survival by having adjuvant therapy, additional chemotherapy treatment after breast cancer surgery. Four studies published in 1989 by the New England Journal of Medicine indicate that women with early stages of breast cancer who receive adjuvant therapy are more likely to stay cancer-free for four years. Some physicians are skeptical about adjuvant therapy. They point out that the studies do not prove that a woman's long-term survival is improved, and that the often severe side effects of chemotherapy decrease quality of life. A statistical technique employed by Richard Peto, director of Oxford's Cancer Studies Unit, was used to project long-term survival rates among women with early stages of breast cancer who received adjuvant therapy. The resulting data suggested, among other things, that additional therapy following breast cancer surgery can increase a woman's life by 10 years. Taxol, a powerful anticancer drug extracted from the yew tree, is now being tested as an adjuvant therapy treatment. While taxol is known mainly for its ability to fight ovarian cancer, researchers say preliminary findings suggest that the drug may also help women with breast cancer.

Farnsworth, N.R. 1992. The Importance of Plant-Derived Pharmaceuticals and Methods Used for Identifying Plants for Drug Discovery. Program for Collaborative Research in the Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, Illinois, 60612.

Abstract - This presentation will provide an overview of the importance of plant-derived pharmaceuticals in the USA and globally. More than 120 plant-derived compounds of known structure are currently used as drugs throughout the world. Many of these are not used in the USA, but are of established medical benefit. These 120 compounds are derived from only 90 species of plants, most from temperate zones of the world

and 74% of them were discovered by chemists who were attempting to isolate and identify the active principles of the plants based on folkloric (ethnomedical) uses. The value of ethnomedical information as a predictor of experimental biological activity will be examined and other methods of selecting plants for specific biological activities will be delineated. Some examples of plant-derived bioactive compounds that have provided new "unnatural" drugs based on analog preparation will be presented. Considering that more than 250,000 species of higher plants exist on this planet, more rational approaches than blind screening after random collection of plants seem to be worthy of using.

Fiscus, James W.; McMahon, Donna. 1991. Medical science races to increase output of taxol. Portland: The Oregonian. November [n.d.]. Section B.

Abstract - This article discusses efforts by scientists to synthesize taxol, with an eye toward full clinical use. Taxol is currently used in large-scale phase III trials for the treatment of ovarian cancer and has been made available to 39 U.S. cancer treatment centers for care of women with epithelial ovarian cancer. There is concern that public expectations for taxol may be too high, and that the drug has been oversold. Taxol is in short supply, and this has slowed research. When taxol is accepted for general clinical use, far larger supplies will be needed. An analogue of taxol, taxotere, in which the side chain is added to baccatin III extracted from the European yew is being tested in the United States and in France. Baccatin III is extracted from leaves while taxol is extracted from bark. ESCAgenetics Corp. is working to produce taxol from tissue cultures.

G

Green, Pat ; Ward, Roger. 1991. Yew Sprout Assessment, Nez Perce National Forest, Idaho. Report on file with yew technical committee. Portland, OR: USDA Forest Service, Pacific Northwest Region, Portland, OR. 1 p.

Green and Ward conclude from their observations that sprouting is moderately reliable from stumps of yew unaffected by fire. However, under the browse regime on the Nez Perce, there is no indication that sprouts will do more than maintain a precarious viability for the plant, with little hope of recovering reproductive capacity. Tree form yew that is above browse height seems to be the primary agent for sexual reproduction, and current levels of browsing on smaller yew suggests that moose population pressure will prevent smaller yew form growing out of browse height. It looks like significant if temporary declines in moose populations would be required to allow new yew plants to develop the tree-like form that is useful for bark harvest.

Greenup, Mel. 1992. Personal Communication. Port-Orford-cedar, Pacific yew, and fungus *Phytophthora lateralis*. March 9. 1 p.

Abstract - Phytophthora lateralis, a fungus normally associated with Port-Orford-cedar has been found on Pacific yew trees in a small area of the Siskiyou and Six Rivers National Forests. Yew trees infected with the fungus were found only in areas where they were mixed with infected Port-Orford-cedar, although the Pacific yew trees appear to be more variable in their susceptibility to infection. Any yew trees found to be infected are being mapped and monitored. All yew inventory crews in Regions 5 and 6 will be briefed on how to identify the fungus. Disease control strategies will be developed for yew trees.

Gunther, Erna. 1945. Ethnobotany of Western Washington. Seattle: University of Washington Press. P. 16.

Abstract - This text on Native American use and knowledge of indigenous plants includes an entry on Western yew. This tree was used by at least eight Pacific Northwest Indian tribes for various purposes. The Klallam, Samish, and Swinomish dried yew needles and used them as a tobacco substitute for smoking. Many tribes used yew wood for constructing bows, arrows and other weapons. Yew was also used as a medicine. The tree symbolized strength and power. Swinomish youths would rub themselves with yew sticks and boughs to impart strength. The Chehalis soaked crushed yew leaves in water and bathed children and elderly persons in it. The Klallam used yew leaves to make a tea, which they drank to heal internal ailments and injuries. The Quinalt made a tea out of dried, peeled yew bark, which was ingested as a lung medicine.

H

Hall, Frederick C. 1989. Plant association and management guide for the Ochoco and southern Blue Mountain areas. United States Department of Agriculture, Forest Service, Pacific Northwest Region, R6 Ecol TP-000-90.

Abstract - This guide provides information on vegetation in both forest and non-forest settings in the Ochoco and southern Blue Mountain areas. A key is provided to be applicable to vegetation in most stages of disturbance such as poor and very poor forage rating, clearcuts, and burns. Plant association descriptions are organized by similarity in dominant plants and environment. A species list is included, alphabetized both by Genus and common name. Summary tables are provided concerning the non-forest environments, forest productivity, tree species productivity. Also shown is an association table. Finally, an "indicator species" section is divided into dryland vegetation and wetland vegetation.

Hall, Judy; Alaback, Paul. [n.d.]. Native plants of southern Alaska. University of Alaska Press. [only have 1 page].

Abstract - The included page provides a brief description of *Taxus brevifolia,* the Western yew. Locations where the yew can be found, as well as a few comments are also shown.

Hartzell, Hal. 1991. The yew tree - A thousand whispers. (Biography of a Species.) Hulogosi Press. 319 p.

Abstract - Originally written about the myth, legend, lore, historical, and poetical associations of the yew tree in 1983, this book was rewritten to include several chapters about the taxol issue, as well as additional mythical and poetical allusions, and historical, geographical, and botanical information. It includes an afterword by Jerry Rust, and three appendices listing: yew trees larger than 20 feet in girth in England and Wales; notable topiary and hedges in England; and yew species and cultivars.

Hauser Northwest, Inc. [n.d.]. Pacific yew bark for cancer research and treatment [Brochure]. Cottage Grove, OR.

Abstract - This brochure briefly discusses the Pacific yew as the source of the new cancer drug, taxol. The National Cancer Institute is working jointly with Bristol-Myers Squibb Company to develop this drug. Because of their success at developing other medically valuable drugs from natural substances, Hauser Chemical Research, Inc. has been selected as the supplier of yew bark and taxol. Current taxol collecting techniques and developments are also discussed.

Heiken, Doug. 1992. Federal management of an emerging resource: the Pacific yew. Unpublished. Draft. January. 87 p.

Abstract - This paper discusses the need to balance federal management of the Pacific yew with creating a sustainable yew management program. The paper critically analyzes the response of federal agencies to the discovery of yew as a valuable resource on federal lands. The paper is divided into thirteen sections which include discussions on yew in history, occurrence and ecological function of the Pacific yew, supplying the anticipated future demand for taxol, the role of the National Cancer Institute and the Food and Drug Administration in developing and approving taxol, USDA Forest Service management program for yew, Bureau of Land Management yew program, environmental impact analysis and citizen participation under the National Environmental Policy Act, recent congressional action of the Pacific yew, pending litigation on waste of Pacific yew resources, and poaching of yew bark from federal lands.

High Country News. 1991. Drug firm gets a monopoly on harvesting yew trees. August 26.

Abstract - The Forest Service and Bureau of Land Management have signed agreements with Bristol-Myers Squibb giving the pharmaceutical giant first rights to all Pacific yew trees (needed for extraction of taxol) on federal lands for at least five years. In exchange, the drug company will fund an inventory of the trees on federal lands, develop yew conservation guidelines, and conduct research toward the establishment of yew plantations. A current issue is that the old growth where most Pacific yews are found will be destroyed in the search for the drug. The drug company plans to extract taxol from yew needles and other sources eventually, but for the time being, yew bark is the only source of the drug.

Hoadley, R. Bruce. 1990. Identifying wood: accurate results with simple tools. The Taunton Press. Newtown, CT. 223 p.

Abstract - Pacific yew (*T. brevifolia*) wood is easily distinguishable from other woods. Its texture is extremely fine with orange to russet heartwood. Pacific yew is indistinguishable from that of European or common yew.

Holmes, John. 1991. Trying to save a lifesaver. Insight. 7(36): 30-31.

Abstract - This article discusses the controversy taking place in the forests of the Pacific Northwest. The Pacific yew tree is the source of a new cancer-fighting drug called taxol. The drug is found in the bark of the yew. Environmentalists fear that the sudden demand for yew trees and taxol will destroy the species. Although scientists are close to synthesizing taxol in the laboratory, conservation groups worry that the tree will be wiped out before synthesis is perfected.

Horwitz, Susan B. 1992. Taxol: mechanisms of action and resistance. Department of Molecular Pharmacology. Bronx, NY: Albert Einstein College of Medicine.

Abstract - Taxol is emerging as a drug that is very likely to play a major role in cancer chemotherapy in the future. It is demonstrating extremely encouraging activity in human advanced ovarian cancer and metastatic breast carcinoma. The drug is isolated from the bark of *Taxus brevifolia*, the western yew, which is a slow growing evergreen species found in the ancient forests of the Pacific northwest. In addition to having a novel chemical structure, taxol has a unique mechanism of action. The drug induces the formation of cytoplasmic bundles of microtubules in cells and stabilizes the microtubule polymer against depolymerization. A murine tumor cell line, J774.2, selected for resistance to taxol, displays the multidrug resistance phenotype including the overproduction of P-glycoprotein, a drug-efflux pump responsible for maintaining low levels of taxol within the resistant cells. Compared to the parental drug-sensitive cell line, the taxol-resistant cell line also synthesizes increased quantities of tubulin, the subunits of microtubules.

J

Jaffe, Mark. 1992. Killing the cure. The Philadelphia Inquirer Magazine. February 23: 16-24.

Abstract - The old growth forests of the Pacific Northwest provide the backdrop for this article, which discusses the Pacific yew tree as the main source of the cancer-fighting drug, taxol. The author gives a comprehensive history of taxol discovery and research, from the early 1960's when it was first discovered, to the present. A U.S. Department of Agriculture botanist first identified taxol in 1962 while working with the National Cancer Institute in a combined-effort search for natural anticancer drugs. Taxol did not get much widespread attention until 1978 when researchers realized that it did not behave like other cancer-fighting drugs. Instead of stopping cell division by blocking the growth of microtubules, small hollow tubes that give cells shape and are essential for cell division, taxol actually increases microtubule production. This results in the cancer cell actually being trapped within its own structure, unable to divide and grow. The author goes on to discuss the ways in which the fate of the Pacific yew and other plants containing life-saving medicines are ultimately tied to the fates of their respective ecosystems.

Jagels, Richard. 1986. Woods of the West. Woodenboat. Jan/Feb. No. 68: 103-104.

Abstract - Mentions that *Taxus brevifolia* is a good boat wood and is available along the British Columbia Coast.

Jagels, Richard. 1981. Under-utilized boatbuilding woods. Woodenboat. [Wood Technology Column]. Nov/Dec. No. 42: 123-124.

Abstract - The wood is hard, heavy, and strong, although it has a tendency toward brittleness. It is exceptionally decay resistant. Indians once used this wood extensively for everything from baskets to canoe paddles. Trees are becoming scarce and the wood is often difficult to obtain.

Junod, Tom. 1992. Tree of hope. Life Magazine. May: 71-76.

Abstract - This article discusses the history of taxol discovery and its use as an anticancer drug. Much of the article is told through the eyes of a cancer patient who received taxol. Because of limited supply, researchers currently are testing the drug only on patients with severe cases of ovarian cancer. For many, taxol is the last hope. The article also points out that while clinical trials have shown promise, taxol is not a cancer cure.

K

Kirk, Ruth. 1986. Tradition and change on the Northwest coast. British Columbia Provincial Museum. Seattle: University of Washington Press. 256 p.

Abstract - The weight and strength of yew made it suitable for clubs, bows, and the swordlike beaters that the weavers used to prepare wool. To kill a whale, men paddled alongside their prey and struck with toggling mussel-shell harpoon heads mounted on heavy shafts of yew 10 to 15 feet long.

Klinger, David. 1991. Threatened designation inappropriate for Pacific yew; Fish and Wildlife Service cites abundance, few threats. News Brief. United States Fish & Wildlife Service - Region 1. January 9.

Abstract - Insufficient scientific information currently exists to indicate the Pacific yew warrants listing by the Federal Government as a threatened species. The U.S. Fish and Wildlife Service noted further that existing data strongly suggest that listing is not warranted. The decision of January 9, 1991, which incorporates an administrative finding signed in Washington, DC means that the Interior Department agency will not pursue listing of the species at this time.

Krucoff, Carol. 1991. Unlocking the secrets of taxol. Saturday Evening Post. Sept/Oct: 46-47.

Abstract - Dr. Robert Holton, a chemist at Florida State University, has been successful in recreating taxol through a semi-synthetic process. The process involves joining a taxol precursor, Baccatin III, with an easily-synthesized side chain. Holton says, "Nothing is won until taxol's out there and available to patients. The big question now is how do you get large quantities of Baccatin III?" He and other scientists are currently working to synthesize Baccatin III, but for now he says the hundreds of varieties of yew are more likely to be the best source. This article also describes taxol's unique mechanism of action.

Kuehne, Gus. 1991. High Quality Forestry Alternative for Management of the Olympic and Mt. Baker-Snoqualmie National Forests in Washington State. Northwest Independent Forest Manufacturers. Tacoma, Washington. April 16. 5 p.

Abstract - This paper focuses on the concept of High Quality Forestry (H.Q.F.), a proposed system of forest management. Under H.Q.F. management, forest harvest rotations would vary according to habitat needs, economic factors, aesthetic values, recreational uses, and water quality. The paper is divided into seven parts as follows: I. Introduction II. Current Situation III. The Timber Management/Old Growth Habitat Conflict IV. High Quality Forestry Concept V. Reforestation Cuts VI. Intermediate Cuts VII. Summary.

L

Leary, Warren E. [1991] FDA is planning to speed process of approving drugs. New York Times. November 13.

Abstract - The Food and Drug Administration announced plans to speed its drug approval process, including using outside experts to review new drugs and cooperating with other nations to standardize testing and regulation. These plans will hopefully revitalize the agency and "accelerate the availability of drugs for serious and life-threatening illnesses."

Ledig, F. Thomas. 1988. The conservation of diversity in forest trees—why and how should genes be conserved? Bioscience. 38(7): 471-479.

Abstract - This article outlines the scope of gene conservation in relation to wild plants and, most particularly, forest trees. Ledig addresses economic, ecological, and esthetic issues in relationship to gene conservation on an international level. Ledig maintains that breeding has not yet resulted in dangerous uniformity in forestry because most tree breeders strongly emphasize the maintenance of variability (Zobel, 1978). It is important to preserve all genes because it is impossible to predict what may be useful in the future. This takes on special importance now that genes can be transferred between virtually any organisms using recombinant DNA technology. The United States is a great exporter of genes; genetic resources are important to the economy of other countries. Measures that both conserve resources and provide economic benefits can forestall the collapse of our natural ecosystems and buy the world precious time to attack the root of the conservation problem—population growth and concomitant poverty.

Lemonick, Michael D. 1991. Whose woods are these? Time. December 9: 70 - 75.

Abstract - This article discusses the fate of the old growth forests. The author states that the national forests by definition belong to the American public, and it is the public, not industry lobbyists or agency bureaucrats, that should decide their fate. With increasingly concerned managers inside the Forest Service, environmentalists on the outside and legislators looking sharply over the agency's shoulder, there is reason to hope that the last stands of ancient trees will remain uncut—and that some of their younger cousins will eventually achieve the status of old growth themselves.

Little, Elbert. (Geographer). [n.d.]. Yew Range Map. Distribution of important forest trees of U.S. Volume 1. Map 86-w. 1:200, 1:400.

Abstract - This map shows the range of the native Pacific yew (*Taxus brevifolia*) as it is found from northern California to southeastern Alaska and east to Idaho and western Montana.

M

McCune, Bruce; Allen, T.F.H. 1985. Forest dynamics in the Bitterroot Canyons, Montana. Canadian Journal of Botany. 63: 377-383.

Abstract - Both shade-tolerant and shade-intolerant tree species may dominate young stands in canyon-bottom forests of the Bitterroot Range. Subsequent dynamics depend on growth characteristics of the colonizing species. Thus, much of the compositional variation arises at stand establishment rather than through a replacement process. Pacific yew, however, may require shelter from other species for establishment. Vertical similarity increases with stand age towards a maximum value of about 75%. Although the importance of Pacific yew tends to increase with stand age, convergence on a common climax composition is thwarted by insularity of the canyon bottoms and an average fire cycle that is shorter than the normal longevity of the shortest lived major tree species.

McCune, Bruce; Allen, T.F.H. 1985. Will similar forests develop on similar sites? Canadian Journal of Botany. 63: 367-376

Abstract - This paper discusses the development of old growth mesic forests of the Bitterroot Canyons, western Montana, which tend to be dominated by *Abies grandis, Taxus brevifolia,* and *Thuja plicata*. The paper concludes that similar sites do not necessarily develop similar, relatively stable forests. Differences between site factors and historical factors are discussed. Site factors are defined as factors which are measurable on a specific site during the span of a typical research project. Historical factors are defined as factors which include rarely repeated circumstantial events. Based on the hypothesis, the authors advise caution in using climax vegetation as a standard for comparisons resting upon the assumption that climax composition is determined solely by site characteristics.

Miller, Charles N., Jr. 1988. The origin of modern conifer families. In: Beck, Charles B., ed. Origin and evolution of gymnosperms. New York: Columbia University Press: 448-486.

Abstract - The object of the paper is to provide a synthesis of paleobotanical evidence concerning the origin of modern conifer families. Over 100 equally parsimonious trees resulted from the parsimony analysis of data. Despite evidence of homoplasy in many of the characters, there is only one basic form to the trees. Tree variations are due to differences in character state transitions and rearrangements of taxa within the Cupressaceae-Taxodiacea clade. Only two instances of character state reversal or parallelism occur in the equally parsimonious trees leading to the main clades, and only three instances of reversal or parallelism occur within the Araucariaceae- Cephalotaxacea-Pinacceae-Podocarpacceae clade. Thus, the broad trends indicated by the characters have phylogenetic significance at the family level but not at the genus level within the Cupressaceae-Taxodiaceae clade. Character state transitions are given for the family level clades only.

Murray, Marshall D. 1991. The tree that fights cancer. American Forests. July/August: 52-54, 70.

Abstract - Previously considered to be a worthless "weed tree" by timber harvesters, the Pacific yew has recently been discovered to contain an important anticancer drug. The compound, called taxol, is found in the bark of the slow-growing yew, which is most abundant in the old growth forests of the Pacific Northwest. While scientists are trying to develop alternative means of producing taxol, the bark of the Pacific yew continues to be the most viable source. Demand for the drug is rising, and environmentalists fear that the species will be destroyed by overharvest.

N

Nalder, Eric. 1991. Huge firm gets monopoly on promising drug. The Yakima Herald—Republic. December 26: 5C.

Abstract - Under the Drug Orphan Act Bristol-Myers Squibb was given exclusive rights to market taxol for ovarian cancer for seven years. This news article discusses the reasons the government granted a near-monopoly to Bristol-Myers Squibb for the marketing of the drug taxol. Critics say development of the drug has taken much longer than it needed to and cut out competitors who could have done something about the short supply. Concerns about potential unfair pricing once taxol is approved for commercial use are also discussed.

Nalder, Eric. 1991. Late start, rigid bureaucracy delay production. Yakima Herald—Republic. December 27: 7A.

This news article is about the search for alternatives to yew bark as a source for taxol. In spite of suggestions years ago from a botanist and other people involved in taxol, the search for alternatives was delayed for several reasons outlined in this article.

National Cancer Institute. 1991. Taxol briefing questions and answers.

Abstract - This is a list of twenty questions and answers regarding taxol, compiled by the National Cancer Institute. These questions generally cover the basic issues surrounding taxol, agreements with Bristol-Myers Squibb, and current research.

Norse, Elliott A. [n.d.] Statement. Washington, DC: Center for Marine Conservation. 3 p.

Abstract - In this brief statement, Dr. Elliott A. Norse, chief scientist at the Center for Marine Conservation, discusses the Pacific yew as an example warranting both "hope and warning." Norse states that the depletion of the Pacific yew in

clear-cut logging operations is a warning that we are depleting life on the planet and limiting biological diversity. The fact that the yew has only recently been found to contain the cancer-fighting drug taxol is testament to our ignorance of the many plant-derived medicines yet to be discovered. The overall message of Norse's statement is, "Saving biological diversity is saving human lives."

Northwest Independent Forest Manufacturers. [n.d.] Timber harvest program for high quality forestry alternative, harvest schedules, stumpage prices, yields and quality for 150 and 200-year rotations. 17 p.

Abstract - This paper discusses High Quality Forestry (H.Q.F.) an alternative means of forest management. The paper is intended to give direction to the development of H.Q.F. and to evaluate the "price, quantity, and quality of timber harvested under the High Quality Forestry alternative." The paper is divided into 10 sections as follows: I. Introduction; II. Rotational Length; III. Commercial Thinning Schedules; IV. Pruning; V. Stumpage Prices for Regeneration Harvests; VI. Stumpage Prices for Commercial Thinnings; VII. Size and Quality; VIII. Total Yield Comparison for 100, 150 and 200 year Rotations; IX. Logging Systems; and X. Summary. Also included are six tables illustrating information on commercial thinning and stumpage prices.

O

Onat, Astrida; Blukis, R.; Hollenbeck, J.L., ed. 1981. Inventory of Native American religious use, practices, localities, and resources. Seattle: Mt. Baker Snoqualmie National Forest.

Yew was used to make bows and spear shafts; a tea was made (by Samish) from the needles to treat arthritis. Yew was used by the Tulalip Tribes to carve the miniature paddles worn on some ceremonial shirts and to make scoring sticks for bone games. The Cowlitz, Nisqually, Puyallup, and Muckleshoot also used yew.

Oregon Association of Nurserymen, Inc. 1991-1992. Directory and buyer's Guide. Conifers, Taxus: 134-135.

Abstract - This publication includes a two-page listing of Oregon nurseries that sell various species of yew trees. Twelve different species are listed.

P

Pennisi, Elizabeth. 1991. Beyond yew: chemists boost taxol yield. Science News. 141: 244.

Abstract - Pennisi attended taxol workshops at the International meeting of the American Chemical Society in San Francisco and listened to scientists present their latest findings. This article briefly discusses advances leading to taxol from other sources which may yield better taxol-based drugs. Paul A. Wender, organic chemist at Stanford University, uses pinene from an inexpensive pine extract found in turpentine to construct a greater part of the taxol molecule. Jeffrey Winkler, a chemist at University of Pennsylvania does the same with a cedar extract. Pierre Potier, chemist at the Institute of Chemistry of Natural Substances in France, uses a European yew taxol precursor to create Taxotere. Robert A. Holton of Florida State University has improved a semisynthetic process using a compound from European yew leaves. Walter E. Goldstein with ESCAgenetics Corp. in California reports that plant cell cultures are another avenue for taxol supplies. All agree that taxol is a crude beginning for a new class of cancer drugs.

Perry, Patrick. 1991. Speaking out—cancer-fighting taxol, yew can do it. Saturday Evening Post. Sept/Oct.

Abstract - This article discusses the potential for a taxol supply from ornamental yew. Baccatin III, a taxol precursor, is found in high concentrations in the English yew, although it is present in varying degrees in all yews. Dr. Ed Croom, an economic botanist and key researcher at the University of Mississippi says scientific reports show some American ornamental yews show significant amounts of taxol comparable to that found in the bark of the wild Pacific yew. Clippings offer a renewable, abundant source of supply. He also comments on the difficulty of harvesting needles from wild yew in comparison to trimming yew needles in organized fields and affirms, "What we are really trying to do is develop a renewable, abundant, and economical source of the drug."

Pierce, John D; Peek, James M. 1984. Moose habitat use and selection patterns in north-central Idaho. Journal of Wildlife Management. 48(4): 1335-1343.

Abstract - Twelve radio-collared moose were monitored in north-central Idaho from January 1979 through April 1982. Moose selected vegetative types where forage was abundant in all seasons. old growth grand fir/ Pacific yew stands were critical moose winter habitat. Winter habitat use patterns did not differ among years even though snowfall varied dramatically. Even-aged pole timber stands and open areas, including clear-cuts and lakes, were used most by moose during summer. During deep snow periods, preferred moose habitat was characterized by dense cover and abundant forage.

Plenert, Marvin L. 1990. Memorandum on administrative 90-day petition finding for the Pacific yew *(Taxus brevifolia)*. United States Department of the Interior, Fish and Wildlife Service. December 21. 10 p.

Abstract - This memorandum constitutes the 90-day finding for the petition, in accordance with Section 4(b) 3(a) of the Act. This finding was prepared by the staff of the Sacramento Field Station and reviewed by the Portland Regional Office. The Service responded to each of the main points of the petitioners.

Polsky, B. 1991. Satellite images assist drug makers in cancer quest. Space News. October 28-November 3.

Abstract - Pacific Meridian Resources, a natural resources consulting firm, is helping the USDA to locate Pacific yew trees on public lands. Under a contract with the Forest Service, the company is using Landsat remote sensing devices to identify places where yew trees are likely to be found. The remote sensing satellites are owned and operated by the National Oceanic and Atmospheric Administration. The data collected is used to make maps.

Potier, P.; Gueritte-Voegelein, D. 1992. Taxotere: discovery, structural studies and uses. Guenard Institut de Chimie des Substances Naturelles. CNRS-91198 Gif sur Tvette-France.

Abstract - Taxotere[r] is a new synthetic analogue of taxol which was selected on the basis of its enhanced inhibition of cold disassembly of microtubules compared to taxol. Now in phase II clinical trials, Taxotere[r] is prepared from 10-deacetyl baccatin III, a compound isolated from the needles of the European yew tree (*Taxus baccata* L.). Taxol can also be easily prepared from the same naturally occurring compound. The production of taxane derivatives following this process is only limited by the accessibility of yew tree leaves. This process constitutes a much more interesting and ecological approach than that consisting in extracting taxol from the trunk bark which requires destruction of entire yew forests. From the same precursor a number of analogues have been prepared. Comparison of the conformations obtained by molecular modelization and NMR experiments on these different derivatives allowed us to determine the most likely "active" conformation. At present time, Taxotere[r], is the best compound of the taxol series in the clinic owing to its better solubility and bioavailability.

Price, Robert A. 1990. The genera of *Taxacacea* in the southeastern United States. Journal of the Arnold Arboretum. 71: 69-91.

Abstract - This paper gives a technical overview of the genera *Taxacacea* (yew) as it is found in the southeastern United States. Plant morphology, range, natural history, and plant chemistry are discussed.

R

Richardson, Sherri. 1991. Pacific yew: a miracle cancer cure? Forestry Research West. April: 11-15.

Abstract - This article identifies the Pacific yew as the source of a life-saving drug, taxol. The Pacific yew is an understory species found along the Pacific coast from Alaska to central California, and is characterized by its relatively slow growth. One tree, on the average, provides 40 pounds of green bark that, when dried, weighs 19 pounds. 60,000 pounds of dried bark produces about nine pounds of taxol. Long-term viability of the species may still be a problem, especially where extensive areas of forest are managed on short-rotations and harvested by clearcutting. Attempts to synthesize taxol in the laboratory have not been successful. Many people believe it may not be possible. The USDA is also in the process of filing a patent to produce taxol from tissue cultures.

Robbins, C.T; Mole, S; Hagerman, A.E; Hanley, T.A. 1987. Role of tannins in defending plants against ruminants: reduction in dry matter digestion. Ecology. 68(6): 1606-1615.

Abstract - Polyphenolic allelochemicals, such as tannins, are widely thought to reduce the digestibility of plants consumed by herbivores by binding to digestive enzymes and dietary proteins. While the apparent digestibility of protein and, therefore, cell soubles is reduced in mule deer and white-tailed deer consuming tanniferous forages, digestion of the plant cell wall is not reduced beyond that predicted from its content of lignin, cutin, and silica. The occurrence of such proteins in ruminants is reported here for the first time. The saliva composition of mule deer and domestic cattle and sheep are compared, and the higher potential of the deer saliva to neutralize tannins may minimize fecal nitrogen losses by maximizing the efficiency of tannin-binding per unit of protein and may reduce the absorption of hydrolyzable.

Rowinsky, Eric K.; Cazenave, Lorraine A.; Donehower, Ross C. 1990. Taxol: a novel investigational anti-microtubule agent. Journal of the National Cancer Institute. 82(15): 1247-1259.

Abstract - Microtubules are among the most strategic subcellular targets of anticancer chemotherapeutics. Despite this, new anti-microtubule agents have not been introduced over the last several decades—until taxol. Taxol induces tubulin polymerization and forms extremely stable and nonfunction microtubules. Taxol has demonstrated broad activity in preclinical screening studies, and anti-neoplastic activity has been observed in several classically refractory tumors (including phase II cisplatin-resistant ovarian carcinoma and phase I malignant melanoma and non-small cell lung carcinoma). Taxol's structural complexity has hampered the development of feasible processes for synthesis. Its scarcity has limited the use of a broad-scale screening approach. Taxol's unique mechanism of action, its pre-clinical anti-tumor activity, and tumor responses in early clinical trials have generated renewed interested in pursuing its development.

Rowinsky, Eric K; Donehower, Ross C. 1991. Taxol: twenty years later, the story unfolds. Journal of the National Cancer Institute. 83(24): 1778-1781.

Abstract - This editorial makes the case that the value of taxol to cancer patients and to society as a whole overshadows all negative aspects of the process that has led to taxol discovery and production. The authors state that while governmental involvement in a process that promises great potential for commercial value may be viewed critically by some, it is a small price to pay for the development of such an important drug. "The preliminary and extremely encouraging success with taxol should also serve as an inspiration to those involved in drug development to be perseverant and tenacious . . ."

Rust, Jerry. 1991. The yew - a renewable economic resource for the Pacific Northwest. Presented to the Native Yew Conservation Committee. January 18.

Abstract - The yew tree and its derivatives, most notably taxol, represent an opportunity for sustainable economic development in the Pacific Northwest. This paper outlines an approach to develop a multi-faceted industry niche based on the yew, and will attempt to identify specific actions that could lead to the establishment of several thousand jobs and guarantee a renewable source of the promising anticancer treatment utilizing taxol. The approach suggested in this paper suggests conserving and utilizing the existing native yew stands on a sustained yield basis. Jobs would be created in bark <u>and</u> foliage collection; extraction of taxol; research and development; and forest conservation. Further job opportunities exist in developing a wood product line for finished yew products and in stimulating tourism and other forms of economic development.

S

Schepartz, Saul A., Ph.D. 1991. Yews & taxol: issues surrounding a new lifeline for cancer patients, guest column. NIH/OCC. Unknown Source: 3-4.

Abstract - This is an authoritative description of taxol and the scientific basis for encouraging its development. Taxol was isolated from the Pacific Yew tree. The problem is procurement of adequate quantities of the drug. The current source of taxol is the bark of the Pacific yew. It is imperative that alternative and renewable sources of the drug be developed to ensure species preservation due to the logistical and technical problems involved in collecting and processing large quantities of bark. The major emphasis in developing alternatives will be on production of taxol from the needles of Pacific yew and/or other *Taxus* species. Chemical stability of the compound in the needles is highly dependent upon the method of drying, which is not the case with the bark. Other approaches are also being investigated.

Scher, Stanley. [n.d.]. Conserving the Pacific yew. Fremontia. 19(4): 15-18.

Abstract - This article discusses the range of various species of yew, including Florida yew and Mexican yew. The author also discusses current threats to yew populations, yew conservation and management, and future yew management strategies.

Scher, Stanley; Jimerson, Thomas M. 1989. Does fire regime determine the distribution of Pacific yew in forested watersheds? General Technical Report, United States Department of Agriculture, Forest Service, PSW-109: 160-161.

Abstract - This article defines the habitat of the *Taxus brevifolia* and assesses the role of fire in limiting the distribution of this heat-sensitive species. Studies of TABR distribution in more than 950 plots suggest that proximity to water, vegetative cover, slope position, and elevation are major determinants of TABR on the Six Rivers and Klamath National Forests in northern California. Areas with high frequencies of fire have low frequencies of TABR occurrence.

Scher, Stanley; Jimerson, Thomas M. 1989. Unpublished. Factors influencing the distribution of Pacific yew in northwest California. 27 p.

Abstract - Factors determining the distribution of Pacific yew were assessed on the Six Rivers and Klamath National Forests in northwestern California. Study sites included late, mature, and early seral stages of the major conifer series within the study area. Of the 951 plots surveyed, 143 contained Pacific yew. This species occurred most frequently in late seral stage stands of the Port-Orford-cedar series (20 percent) followed by the Douglas-fir series (13 percent) white fir/red fir series (4 percent) and the Douglas-fir plantations (2 percent). Significant differences in stand age were noted for stands with and without Pacific yew in the Douglas-fir, white and red fir series. The primary factors influencing Pacific yew distribution were: stand age, fire frequency, slope position, slope shape, proximity to water, available water holding capacity, and conifer series.

Scher, Stanley; Schwarzschild, Bert. 1989. Pacific yew: a facultative riparian conifer with an uncertain future. General Technical Report. United States Department of Agriculture, Forest Service. PSW-110: 172-175.

Abstract - Increasing demands for Pacific yew bark, the source of an anticancer agent, have generated interest in defining the yew resource and in exploring strategies to conserve this species. The distribution, riparian requirements and ecosystem functions of yew populations in coastal and inland forests of northern California are outlined and alternative approaches to conserving this resource are identified. Efforts to obtain additional information on genetic diversity of yew populations and to ensure careful management of the species are essential for the protection of this resource.

Schweitzer, Robert, M.D. 1990. Letter to Secretary Manuel Lujan. American Cancer Society. September 19. 1 p.

Abstract - This letter urges Interior Secretary Manuel Lujan to take “any and all” actions to protect the Pacific yew tree as a threatened species under the Endangered Species Act. The Pacific yew has recently been identified as an important source of the

cancer-fighting drug taxol, which has shown promise in treating women with ovarian cancer. The American Cancer Society is concerned with ensuring that women diagnosed with ovarian cancer in the future will have access to this drug.

Shadbolt, Doris. 1986. Bill Reid. Seattle/London: University of Washington Press. 192 p.

This publication includes a photograph of a carved yew pendant, painted and inlaid with copper and abalone.

Spies, Thomas A. [n.d.]. Plant species diversity and occurrence in young, mature, and old growth Douglas-fir stands in western Washington and Oregon. PNW-GTR xx. Portland, OR: United States Department of Agriculture, Forest Service, Pacific Northwest Research Station. 42 p.

Abstract - The objective of the study was to characterize differences in vascular plant diversity and species abundance among young, mature, and old growth Douglas-fir forest. A chronosequence of Douglas-fir stands was sampled in each of three physiographic provinces: southwestern Washington Cascades; western Oregon Cascades; and southern Oregon Cascades. The cover of all vascular plants was recorded in 177 stands each consisting of 4-to-5 200 m^2 plots. Measures of species diversity were calculated for the overstory and understory strata of each stand. Species diversity in each province showed an age-class effect ($p<0.1$) in 6 of the 12 tests performed. Diversity remained constant or increased slowly with age class. Frequency of occurrence of species showed an age class effect ($p<0.1$) in 15-to-20 percent of understory species tested in the provinces. Similar results were obtained in analyses based on species cover, though relative differences between old growth and the other age classes were greater. Species occurring with greatest frequency and abundance in old growth included: *Taxus brevifolia*, *Cornus canadensis* and *Tiarella trifoliata* var *unifoliata*, understory herbs, and *Lobaria*.

Stevens, Williams K. 1992. Shamans and scientists seek cures in plants. New York Times. January 28. B5-B9.

Abstract - This article discusses the recent burst of pharmaceutical research aimed at uncovering botanical secrets held by native peoples around the world. Improved technology is allowing companies to screen plants for medicinal agents around the clock. The problem lies in the fact that as the earth becomes more populated, natural habitats are destroyed and species become extinct even before they are discovered. This problem is epecially troublesome in the South American rainforests. Conservationists, government agencies, and pharmaceutical companies are finally beginning to join forces to protect the rain forests and, in turn, protect important botanical medicines. Companies are now sending ethnobotanists to native healers around the world to question them about various plants. The plants are then collected and screened for medicinal activity. If the plant is found to contain an active medicinal compound, the researchers isolate the active ingredient and attempt to secure a patent. In one research project in India, scientists used a 2,500 year-old Sanscrit medical text to find a compound helpful in combatting high cholesterol.

Stewart, Wilson N. 1983. Paleobotany and the evolution of plants. New York: Cambridge University Press. p. 348, 360, 361.

Abstract - Included is a table showing suggested origins and relationships of Ginkgoales, Gnetopsida, and major groups of coniferophytes, and their distribution in geological time. Also included are brief discussions of *Cephalotaxaceae*, Taxales, and Gnetopsida.

Stickney, Peter F. 1980. Data base for post-fire succession, first six to nine years, in Montana Larch-fir forests. General Technical Report INT-62. United States Department of Agriculture, Forest Service, Intermountain Forest and Range Experiment Station. Ogden, UT.

Abstract - Shown are a collection of tables in which *Taxus brevifolia* is found. The burning units included are North - 6, North - 8, and East - 6 of Miller Creek.

Stickney, Peter F. 1981. Vegetative recovery and development. In: DeByle, Norbert V., ed. Clearcutting and fire in the Larch/Douglas-fir forests of western Montana - a multifaceted research summary. General Technical Report INT-99. United States Department of Agriculture, Forest Service, Intermountain Forest and Range Experiment Station.

Abstract - During the first six to nine years after burning, development of vegetation on the 20 units studies at Miller and Newman followed a pattern characteristic for forest succession in the Northern Rocky Mountains. This pattern is initiated by an herb stage, which is followed in turn by shrub and tree stages. In these few years, tree development was non-existent or quite limited on most area. Nowhere did trees attain community dominance. Using cover (crown area) of the predominant life form as the criterion for defining the successional stage, it was found that 9 of the 20 units had progressed to the shrub stage. All others remained in the herb stage.

Suffness, Matthew; Snader, Kenneth M; Cragg, Gordon M; Schepartz, Saul A; Arbuck, Susan; Grever, Michael R. [n.d]. History, Development and Current Status of Taxol at the National Cancer Institute. NCI. Bethesda, Maryland 20892. 36 p.

Abstract - This talk presented at the second NCI workshop on *Taxus* and Taxol is divided into six sections as follows: 1) History and Taxol Development. 2) Status of Clinical Trials. 3) Supply Issues. 4) Research on Production. 5) Basic Research Questions. 6) NCI Research Grants on Taxol.

T

Taxofile. Spring 1992. Newsletter of the Native Yew Conservation Council. 1(1).

Abstract - Includes articles covering the April NYCC public meeting, a recap on events that occurred in 1991, a recap on the 1992 January conference, letters to the NYCC, input to the Pacific Yew Environmental Impact Statement, and more.

Tirmenstein, Debbie. 1991. Pacific yew - *Taxus brevifolia* (a summary paper). Missoula, MT: Fire Effects Information System (FEIS), United States Department of Agriculture, Forest Service Intermountain Fire Sciences Laboratory. 28 p.

Abstract - This paper summarizes many facts and characteristics of the Pacific yew. The sections into which the paper are divided are as follows; Species, Distribution and Occurrence, Value and Use, Botanical and Ecological Characteristics, Fire Ecology, Fire Effects, References, and Bibliography.

Tisdale, Sallie. 1991. Save a life, kill a tree? New York Times. October 26.

Abstract - This editorial argues that people are not more important than the Pacific yew tree. The author cautions us to remember where the yew trees and taxol come from: the forests. Destroy that, she says, and we destroy our future. The article is critical of the commercialization of taxol, yew, and the forests in general. The author argues against the idea that we live in a world where people must wage war against nature. "There is one war and it is people versus people."

Turner, Nancy J. 1982. Food Plants of British Columbia Indians. Part 1/Coastal People. British Columbia Provincial Museum, Handbook No. 34. Second Printing, 264 p.

The Haida at Masset used to eat yew fruit, but noted that if women ate too many they would become sterile. The Fraser River Lillooet in the Interior also used to eat them, but only in small quantities. The Saanich Indians on Vancouver Island dried yew needles and smoked them in a tube of elderberry stem. It was said to make one dizzy.

Turner, Nancy J. 1979. Plants in British Columbia, Indian Technology. British Columbia Province Museum. Handbook No. 38.

Abstract - The heavy, close-grained wood of yew is well known for its strength and durability. It was prized by all native people within the range of the tree, and was frequently taken into areas where it did not grow naturally. It was used to make bows, wedges, clubs, saddles, digging sticks, adz handles, and harpoon shafts, which were required to handle considerable stress. Although tough and hard, it carves fairly easily taking a high polish. As an indication of its importance as a carving material, yew is called "bow plant" or "bow" in a number of Indian languages including Haida Halkomelem and Lillooet. It is called the "wedge plant" in Sechelt, Squamish, and Mootka. Yew wood was also used to make a variety of other objects including: mat-sewing needles, awls, fish hooks, knives, dishes, spoons, spears, etc.

U

USDA, Forest Service. 1984. Regional guide for the Pacific Northwest Region. United States Department of Agriculture, Forest Service, Pacific Northwest Region.

Abstract - The primary purpose of this Regional Guide is to provide national and Regional direction to the 19 National Forests within the Pacific Northwest Region for land and resource management planning efforts. The Guide facilitates National Forest planning by providing Regional standards and guidelines for addressing major issues and management concerns and by displaying tentative resource objectives for each National Forest, based on objectives that were assigned to the Region as a whole in the National RPA Recommended Program.

USDA, Forest Service. 1990. A paper provided in response to the petition to list Pacific yew as a threatened species. United States Department of Agriculture, Forest Service. November 26. 11 p.

Abstract - This paper is a summary of current information about both the species Pacific yew and the implications for the species with respect to the demand for taxol. Addressed in this summary are: the petition to list Pacific yew as a threatened species; taxol as a cancer drug; range of Pacific yew; silvics of Pacific yew; autecology; estimates of availability; current harvest of Pacific yew for bark; future demand for Pacific yew bark; inventory needs; current national forest policies; and management consideration.

USDA, Forest Service. 1991. Emphasis program. New perspectives in forestry: an ecological path for forest management. United States Department of Agriculture, Pacific Northwest Research Station. 2p.

Abstract - This program is the Pacific Northwest's new program for research, development, demonstration, and applications using an interdisciplinary approach to develop alternative ways to manage forest lands. More complete incorporation of ecological and social values into stand and landscape level practices is expected to reduce future conflicts among competing economic, social, and environmental interests.

USDA, Forest Service. 1991. The Pacific yew and taxol. Briefing Paper. United States Department of Agriculture, Forest Service, Pacific Northwest Research Station. February 25.

Abstract - This briefing paper discusses both the Pacific yew and taxol, an extract of tissues from the Pacific yew. Taxol is first discussed as a relatively successful cancer fighting drug. As the production of taxol from other sources increases, the dependence on bark from "native" Pacific yew is expected to be reduced greatly. Characteristics of the Pacific yew are also provided, including the range the Pacific yew extends, its shrub and tree occurrences, its dioeciousity, and its slow growth. The current harvest of Pacific yew bark is also discussed.

USDA, Forest Service. 1991. Desk guide to tribal government relations. Tribal Relations Advisory Group. United States Department of Agriculture, Forest Service, Pacific Northwest Region. September. 56 p.

In response to a growing number of questions regarding our government-to-government relations with Indian Tribes in Region 6, this publication has been developed to assist the Region as a whole to better understand the special relationship the United States and its Agencies have with Indian Tribes and tribal governments. This desk Guide is designed to be a reference book and the information will be updated on a regular basis. The basic Forest Service program areas associated with Indian Tribes are: (1) treaty rights; (2) cultural values; (3) the National Forest Management Act, and (4) individual Indian rights. This Guide focuses on the Treaty and Other Rights and Tribal Governments aspects of Forest Service responsibilities.

USDA, Forest Service. 1992. An interim guide to the conservation and management of Pacific yew. United States Department of Agriculture, Forest Service, Pacific Northwest Region. March. 78 p.

Abstract - This guide is designed to assist land managers with Pacific yew conservation and management. The Pacific yew has recently been found to contain taxol, an important cancer-fighting drug. Until this discovery, the Pacific yew was essentially ignored by modern society as an important tree species. In thé future, taxol is expected to become available through laboratory synthesis and production in non-forest environments, but for the short term, the Pacific yew will be in high demand as a source of taxol. The guide is divided into four parts: I. Executive Summary and Introduction; II. Pacific Yew Biology; III. Yew Management; and IV. Research Needs and Priorities. The appendixes include a list of plant associations and a glossary.

USDA, Forest Service. 1992. Environmental assessment for the 1992 yew bark harvest outside timber sale areas. Nez Perce National Forest, Idaho County, Idaho.

Abstract - Three alternatives for a 1992 yew bark harvest program outside timber sale areas were developed by an interdisciplinary team. **Alternative one** is the No Action alternative and allows yew bark harvest only within existing timber sale harvest units and road clearing limits. **Alternative two**, the proposed action and selected alternative, would allow harvest on about 814 acres. Non-yew forage would be improved on moose winter range, some of which show heavy use by moose yet lacks forage other than yew. This alternative is also designed to lessen adverse effects on wildlife security and to harvest on steeper slopes in order to avoid areas preferred by wintering moose. **Alternative three** allows yew harvest on about 762 acres. Moose forage production would be emphasized on sites managed primarily for timber production rather than on identified moose winter range. This alternative would discourage use of forage by moose and elk along Road 286 and reduce moose and elk vulnerability to hunters and poachers. Yew harvest would be generally located on gentle slopes preferred by wintering moose.

USDHHS, Food and Drug Administration. 1988. From Test Tube to Patient: New Drug Development in the United States. FDA Consumer (Special Report). Rockville, MD. January. 58 p.

Abstract - This issue is a compilation of articles covering the many different aspects of new drug development. They include a section on how the Food and Drug Administration approves new drugs as well as information on drug legislation. One article provides a general timeline table for development and approval of a new drug; it takes an average of 100 months from initial synthesis to approval of the New Drug Application. There are articles on laboratory and animal studies, and human clinical trials.

USDHHS, Food and Drug Administration. 1987. Guideline for the Format and Content of the Chemistry, Manufacturing and Controls Section of an Application. (Special Report). Rockville, MD. February. 11 p.

Abstract - This guideline is intended to assist drug firms in preparing the chemistry, manufacturing, and controls technical section of applications to market new drugs or antibiotics for human use.

USDI, Fish and Wildlife Service. 1990. Memorandum. Administrative 90-day petition finding for the Pacific yew. *(Taxus brevifolia)* December 21. 10 p.

Abstract - Based on numerous studies, reports, documents, available literature, field sighting records, and interviews, the Fish and Wildlife Service determined that no substantial data exists to warrant listing the Pacific yew as a threatened species under the Endangered Species Act.

USDI, Bureau of Land Management. 1991. Information Bulletin. Oregon State Office, Portland, OR. December 26. 5 p.

Abstract - This news bulletin discusses current and planned Pacific yew program activities for the Bureau of Land management. The bulletin includes a list of Annual Pacific Yew Program Plans (APYPP) a summary of the draft PYPP, work summaries for the PYPP task forces and committees, and a list of names and addresses of Pacific yew coordinators for Oregon and Washington.

V

Vidensek, N.; Lim, P.; Campbell, A.; Carlson, C. 1990. Taxol Content in Bark, Wood Root, Leaf, Twig, and Seedling From Several *Taxus* Species. Journal of Natural Products. 53(6): 1609-1610.

Abstract - Taxol content in various parts of several *Taxus* species have been determined. The weight percent ranged from 0.00003 to 0.069.

Viereck, Leslie A.; Little, Elbert L., Jr. [n.d.] Yew family. In: Alaska trees and shrubs. United States Department of Agriculture, Forest Service, Agriculture Handbook No. 410: 43-45.

Abstract - The yew family is classified as one of three families of conifers or softwoods in Alaska in which the seed plants with seeds partly exposed, not enclosed in fruits. The Pacific yew (Western yew) is a small tree or large shrub of extreme south-end of southeast Alaska. Descriptions of leaves, bark, wood, and seeds are included. The Pacific yew has been found in Alaska only on a few islands near Ketchikan. Descriptions of the pine family (Pinaceae) are also included.

W

Waterman, T.T. 1973. Notes on the Ethnology of the Indians of Puget Sound. Indian Notes and Monographs. Misc. Series No. 59. Museum of the American Indian. Heye Foundation. New York. 97 p.

> The most desirable paddles were made of yew.... The Puget Sound adze is a very effective instrument, used for a wide variety of purposes. It has a very short handle (usually of vine maple, sometimes yew) which is carved to fit the hand. Wedges and the foreshafts of bird spears were also made of yew.

Welsh, Stanley L. [n.d.] Anderson's flora of Alaska and adjacent parts of Canada. 38 p.

> Abstract - This entry provides a brief description of the yew family (Taxaceae), including the Western yew *(Taxus brevifolia)*. A sketch of the Western yew is also shown.

Witherup, Keith M.; Look, Sally A.; Stasko, Michael W., Ghiorzi, Thomas J.; [and others]. 1990. *Taxus* Spp. needles contain amounts of taxol comparable to the bark of *Taxus brevifolia:* analysis and isolation. Journal of Natural Products. 53(5): 1249-1255.

> Abstract - New sources for the antitumor natural product taxol [1] are needed as demands for this promising cancer chemotherapeutic agent increase. Presently, supplies of taxol for clinical studies are obtained from the bark of *Taxus brevifolia*, a potentially limited source. Using analytical methods, the needles and stems of six *Taxus* species have been examined for taxol [1] and 10-deacetylbaccatin III [5], a related compound that can be converted to taxol through a semi-synthetic route. Amounts of taxol comparable to quantities reported from the bark of *T. brevifolia* were found in the needles of four of the *Taxus* species investigated. In addition, taxol was isolated from the needles of one *Taxus* species. Thus, *Taxus* needles may provide a renewable source of this valuable compound.

Wood, Wendell. 1991. Conservationists promise legal action if yew wasted. Statement. Oregon Natural Resources Council. March 11.

Abstract - The Oregon Natural Resources Council announced on March 11 that they would bring legal action against the Willamette National Forest under the Clean Air Act unless the forest fully complies with Oregon's smoke management plan, and better utilizes all downed yew trees discarded in slash piles.

Wright, Michael H. 1988. Stalking the Western Yew. Woodenboat Magazine. May/June: 72-73.

Abstract - Discusses boat construction with *Taxus brevifolia*.

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